Electronic Supplementary Information

Palladium-based coordination cages as dynamic crosslinks in acrylamide hydrogels

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1 Materials and methods

1.1 Materials

Octaethylene glycol (IVALUA, 99%), hexaethylene glycol (Sigma-Aldrich, 99%), *p*-toluolsulfonylchlorid (Sigma-Aldrich, 99%), KI (Sigma-Aldrich, 99%), Ag_2O (Sigma-Aldrich, 99%), 3,5-dibromophenol (Sigma-Aldrich, 97%), $Cs_2(CO_3)$ (Sigma-Aldrich, 99%), 3-pyridineboronic acid pinacol ester (Sigma-Aldrich, 97%), 4-pyridineboronic acid pinacol ester (Sigma-Aldrich, 97%), $Pd(PPh_3)_4$ (Sigma-Aldrich, 99%), K_2CO_3 (Sigma-Aldrich, 99%), acryloyl chloride (Sigma-Aldrich, 97%), triethylamine (Sigma-Aldrich, 99%), $Pd(NO_3)_2 \times 2\ H_2O$ (abcr, 99.9%, 41%Pd), $[Pd(CH_3CN)_4](BF_4)_2$ (abcr, 98%), *N*,*N*-dimethylacrylamide (DMA, Sigma-Aldrich, 99%), *N*-hydroxyethyl acrylamide (HEAA, Sigma-Aldrich, 97%), and photo-initiator VA-86 (Fujifilm, 98%) were used as received. *N*-Isopropylacrylamid (NIPAM, Sigma-Aldrich, 97%) was distilled and recrystallized from hexane before use. The polymeric ligand **L1'-PEG$_{4600}$-L1'** was synthesized following literature procedures.[1]

1.2 Methods

NMR spectra were measured on a Bruker Avance Neo spectrometer (^{1}H: 500 MHz, ^{13}C{^{1}H}: 125 MHz) equipped with a CPTCl$_{xyz}$ 5 mm cryoprobe, a Bruker Avance III spectrometer (^{1}H: 400 MHz) equipped with a BBFO$_z$ 5 mm probe and a Bruker Avance III spectrometer (^{1}H: 400 MHz) equipped with a Prodigy BBO 5 mm cryoprobe. The chemical shifts are reported in part per million (ppm) using the solvent residual signal as a reference.

High-resolution mass spectrometry experiments were carried out using a hybrid ion trap-Orbitrap Fourier transform mass spectrometer, Orbitrap Elite (Thermo Scientific) equipped with a TriVersa Nanomate (Advion) nano-electrospray ionization source. Mass spectra were acquired with a minimum resolution setting of 120,000 at 400 *m*/*z*. To reduce the degree of analyte gas phase reactions leading to side products unrelated to solution phase, the transfer capillary temperature was lowered to 50 °C. Experimental parameters were controlled via standard and advanced data acquisition software.

UV irradiation for the photoinitiated polymerization was performed using a UV lamp (CAMAG UV Lamp, 365 nm, 40 W), and the irradiation distance was kept at 1 cm for all reactions.

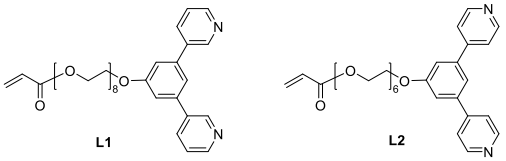
Rheology was performed on a DHR-3 TA Instrument with an 8 mm diameter parallel plate steel geometry. The amplitude sweep measurements were performed from 0.1% to 200% strain at a constant frequency of 1 rad s^{-1}. Frequency sweeps were performed from 1 to 100 rad s^{-1} at 1% strain. For all measurements, the loaded hydrogel samples were immersed in mineral oil to reduce solvent evaporation and hydrogel de-swelling by adsorbing moisture, and the gap was kept constant at 800 µm.

The swelling ability of synthesized hydrogels were measured as follows. To each gel was added 1 mL water, and the gels were allowed to equilibrate at RT for 3 d, at which time the excess water was removed via syringe, and any residual water was wicked away by gently dabbing the gels in the vials. The hydrogels in the vials were weighed, and the dry mass of the gels were weighted after lyophilization. The swelling ratio for each hydrogel was determined by diving the mass of the swollen hydrogel by the dry mass of the hydrogel.

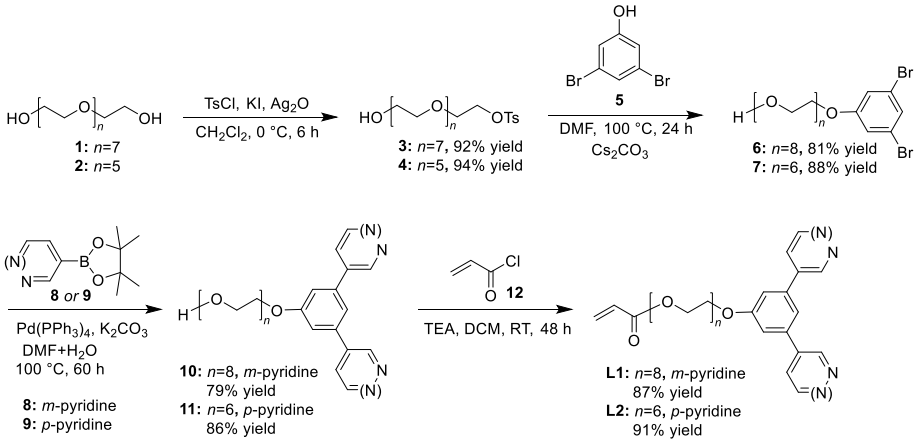
SEM measurements were carried out with freeze-dried hydrogel samples using a scanning electron microscope (Zeiss Merlin). The samples were coated with about 6 nm of iridium to make them conductive before measurements. The SEM electron beam accelerating voltage used was 30 kV.

2 Synthesis and characterizations

2.1 Synthesis and characterization of ligand L1 and L2



Scheme S1. Chemical structures of ligands **L1** and **L2**.



Scheme S2. Synthesis of the ligands **L1** and **L2**.

Synthesis of compounds 3 and 4

The synthesis of compounds **3** and **4** was adapted from a reported procedure.[2] Octaethylene glycol (**1**) or hexaethylene glycol (**2**) (1.0 equiv, 20 mmol) was dissolved in dry dichloromethane (150 mL), and the solution was cooled to 0 °C. Under vigorous stirring, Ag_2O (1.5 equiv, 30 mmol), *p*-toluolsulfonylchlorid (1.05 equiv, 21.0 mmol), and KI (0.2 equiv, 0.40 mmol) were added under inert conditions. After stirring for 2 h, the precipitated silver salts were removed by filtration through a pad of Celite, which was washed thoroughly with ethyl acetate. The combined filtrate was concentrated under vacuum, and the residue was purified by column chromatography (**3**: hexane: ethyl acetate, 1:20; **4**: hexane: ethyl acetate, 1:20). Compound **3** was obtained as a colorless oil (9.70 g, 92%). Compound **4** was obtained as a colorless oil (8.21 g, 94%).

Compound 3: ^{1}H NMR (400 MHz, CD_3CN) δ 7.79 (d, *J*=8.4, 2H), 7.44 (d, *J*=8.2, 2H), 4.15 – 4.09 (m, 2H), 3.62 – 3.46 (m, 30H), 2.76 (t, *J*=5.8, 5.8, 1H), 2.44 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, CD_3CN) δ 146.33, 133.80,

130.97, 128.74, 73.28, 71.13, 71.11, 71.09, 71.00, 70.96, 70.93, 69.14, 61.92, 21.60. HRMS (APCI/QTOF) *m/z*: $[M + Na]^+$ calcd. for $C_{23}H_{40}NaO_{11}S^+$ 547.2184, found 547.2181.

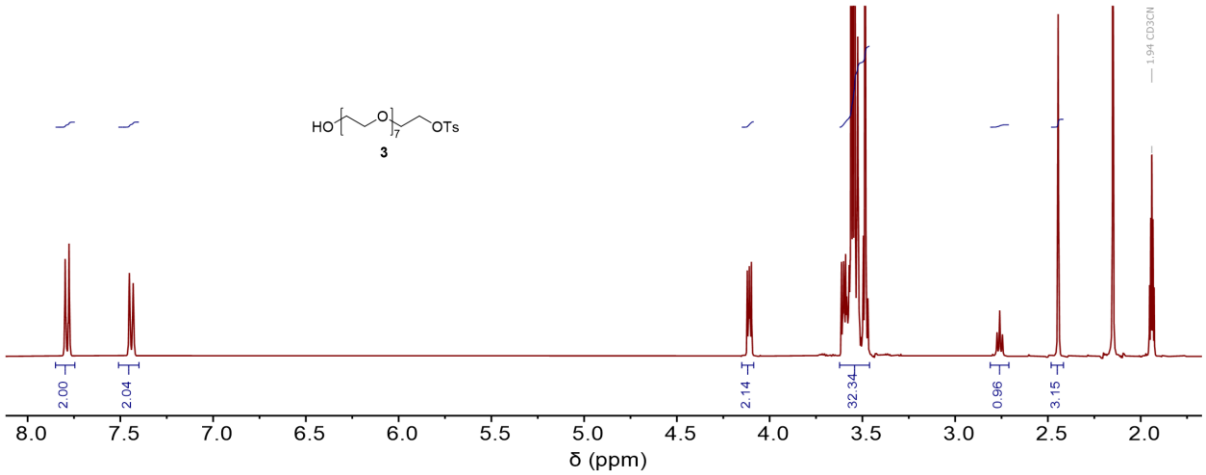


Figure S1. ^1H NMR spectrum (400 MHz, CD_3CN) of compound **3**.

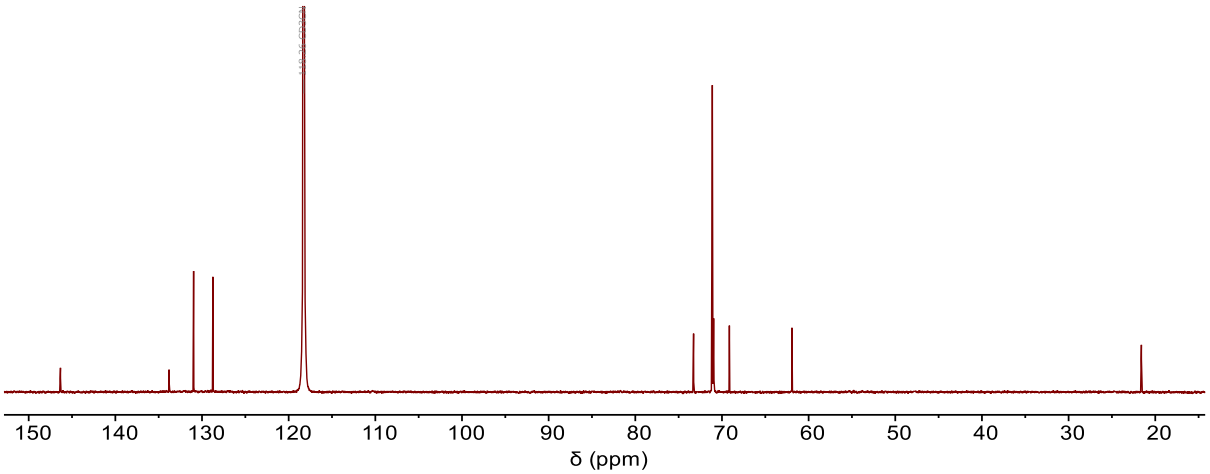


Figure S2. $^{13}C\{^1H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **3**.

Compound 4: ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.76 (d, 2H), 7.47 – 7.41 (dt, 2H), 4.14 – 4.07 (m, 2H), 3.64 – 3.44 (m, 22H), 2.44 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, CD_3CN) δ 146.32, 133.78, 130.96, 128.73, 73.24, 73.22, 71.11, 71.07, 71.05, 71.02, 70.96, 70.94, 70.91, 69.13, 61.92, 21.59. HRMS (ESI/QTOF) *m/z*: $[M + Na]^+$ calcd. for $C_{19}H_{32}NaO_9S^+$ 459.1659, found 459.1676.

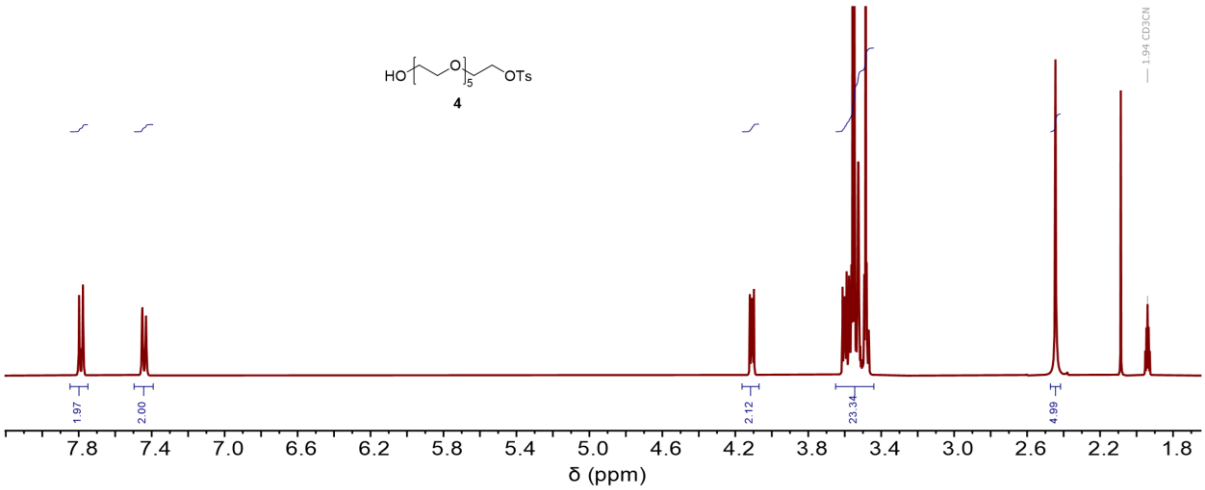


Figure S3. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **4**.

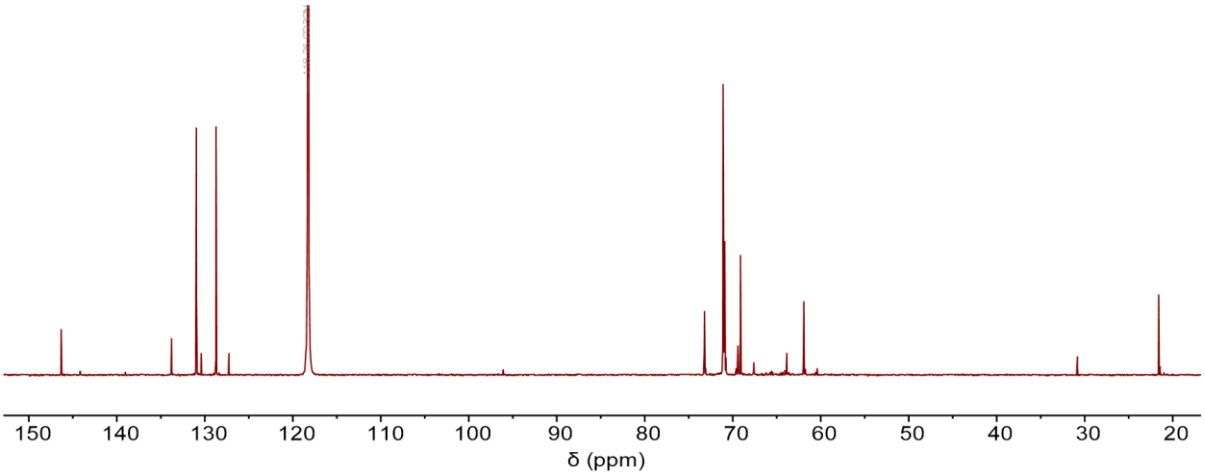


Figure S4. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **4**.

Synthesis of compounds 6 and 7

A solution of 3,5-dibromophenol (**5**, 2.29 g, 1.20 equiv, 9.15 mmol) and Cs_2CO_3 (5.00 g, 2.00 equiv, 15.24 mmol) in DMF (30 mL) was stirred at 100 °C for 2 h under a nitrogen atmosphere. Compound **3** or **4** (1.0 equiv, 7.62 mmol) was then added and the resulting mixture was stirred for 24 h at 100˚C. The reaction was quenched with 30 mL of deionized water and the organic layer was extracted with DCM (3 × 60 mL). The organic phases were combined and washed with water (2 × 60 mL) and brine (3 × 60 mL) before being dried over anhydrous magnesium sulfate and concentrated under vacuum. The residue was purified by chromatography (**6**: ethyl acetate: methanol, 10:1; **7**: ethyl acetate: methanol, 15:1). Compound **6** was obtained as a colorless oil (3.73 g, 81%). Compound **7** was obtained as a colorless oil (3.46 g, 88%).

Compound 6: ^{1}H NMR (400 MHz, CD_3CN) δ 7.32 (t, *J*=1.6, 1.6, 1H), 7.13 (d, *J*=1.6, 2H), 4.13 – 4.08 (m, 2H), 3.78 – 3.73 (m, 2H), 3.63 – 3.52 (m, 26H), 3.50 – 3.46 (m, 2H), 2.80 – 2.73 (m, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ 161.32, 127.03, 123.81, 118.11, 73.27, 71.33, 71.15, 71.11, 71.00, 69.91, 69.33, 61.92. HRMS (APCI/QTOF) *m*/*z*: $[M + H]^+$ calcd. for $C_{22}H_{37}Br_2O_9^+$ 603.0799, found 603.0793.

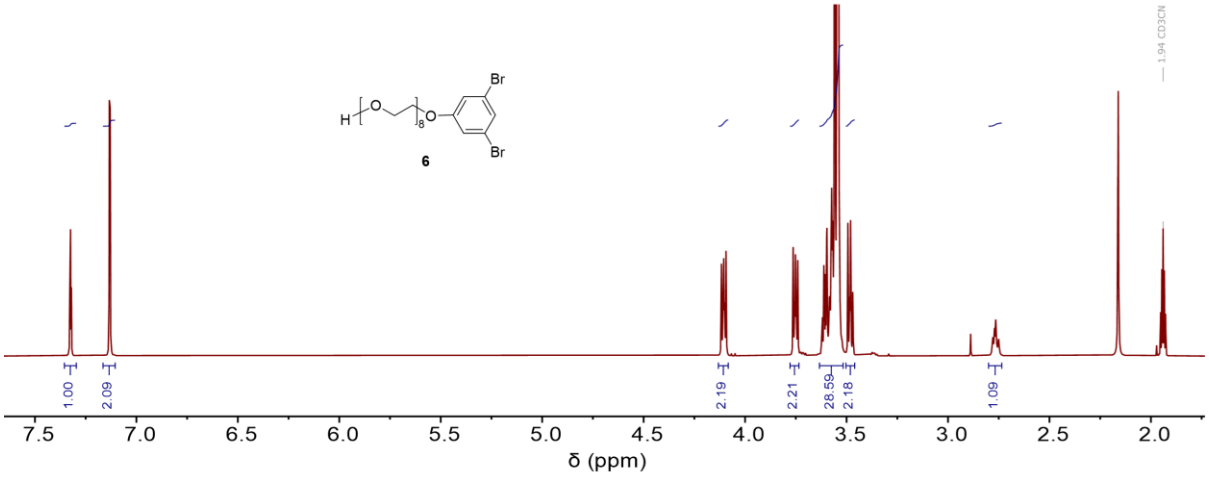


Figure S5. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **6**.

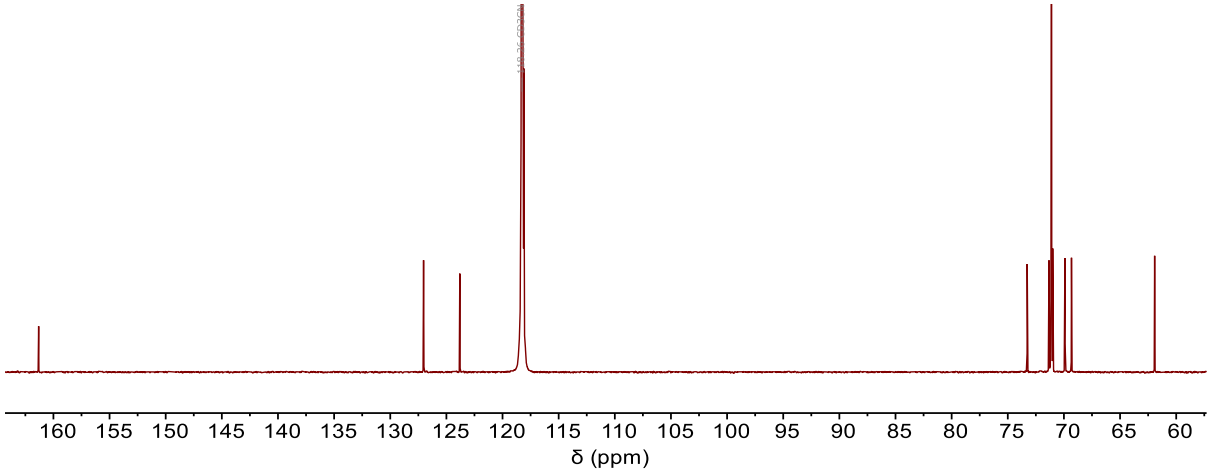


Figure S6. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **6**.

Compound 7: ^{1}H NMR (400 MHz, CD_3CN) δ 7.32 (q, *J*=1.5, 1.5, 1.4, 1H), 7.12 (t, *J*=1.4, 1.4, 2H), 4.13 – 4.07 (m, 2H), 3.78 – 3.72 (m, 2H), 3.63 – 3.52 (m, 18H), 3.50 – 3.45 (m, 2H), 2.80 (d, *J*=5.5, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ 161.29, 127.01, 123.79, 118.08, 73.28, 71.31, 71.14, 71.12, 71.09, 70.98, 69.90, 69.30, 61.92. HRMS (ESI/QTOF) *m*/*z*: $[M + Na]^+$ calcd. for $C_{18}H_{28}Br_2NaO_7^+$ 537.0094, found 537.0114.

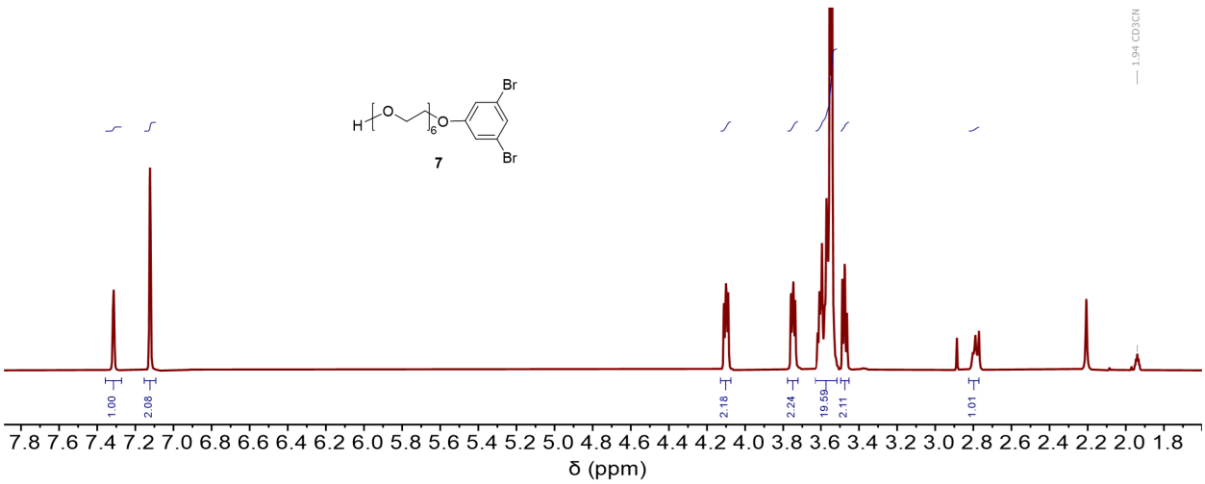


Figure S7. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **7**.

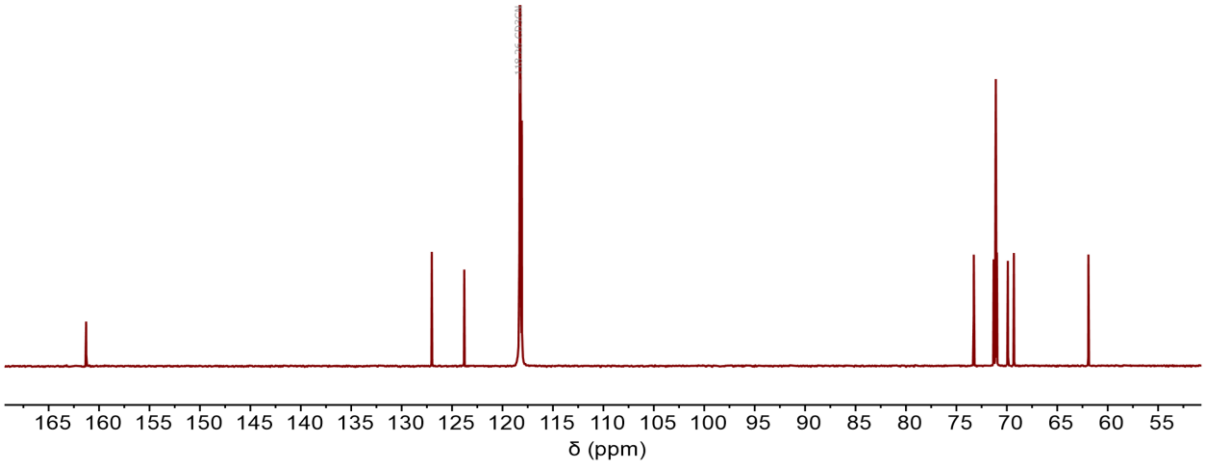


Figure S8. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **7**.

Synthesis of compound 10

Compound **6** (1.81 g, 1.0 equiv, 3.0 mmol), 3-pyridineboronic acid pinacol ester (**8**) (1.48 g, 2.4 equiv, 7.2 mmol), $Pd(PPh_3)_4$ (0.35 g, 0.1 equiv, 0.3 mmol), and K_2CO_3 (4.14 g, 10 equiv, 30 mmol) were added into a 50 mL single-neck round-bottom flask equipped with a magnetic stir bar and capped with a septum. Under a nitrogen atmosphere, DMF (20 mL) along with H_2O (1 mL) were added and the resulting mixture was stirred for 60 h at 100 °C. After cooling to room temperature, the mixture was diluted with chloroform/methanol (10/1, v/v) and filtered through Celite. The filtrate was washed with brine, dried over anhydrous magnesium sulfate, and purified by column chromatography (methanol: ethyl acetate, 1:3). Compound **10** was obtained as a colorless oil (1.42 g, 79%).

^{1}H NMR (400 MHz, CD_3CN) δ 8.94 (d, *J*=1.8, 2H), 8.59 (dd, *J*=4.8, 1.6, 2H), 8.08 (dt, *J*=7.9, 1.7, 1.7, 2H), 7.54 (t, *J*=1.5, 1.5, 1H), 7.44 (ddd, *J*=7.9, 4.8, 0.7, 2H), 7.27 (d, *J*=1.5, 2H), 4.28 (dd, *J*=5.4, 3.8, 2H), 3.94 – 3.79 (m, 2H), 3.65 (dt, *J*=3.9, 2.4, 2.4, 2H), 3.62 – 3.45 (m, 26H), 2.84 (t, *J*=5.7, 5.7, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ 160.99, 149.84, 149.21, 140.98, 136.73, 135.48, 124.60, 119.45, 113.90, 73.29, 71.33, 71.13, 71.09,

71.07, 71.05, 70.95, 70.26, 68.82, 61.88. HRMS (APCI/QTOF) *m/z*: [M + Na]$^+$ calcd. for $C_{32}H_{44}N_2NaO_9^+$ 623.2939, found 623.2942.

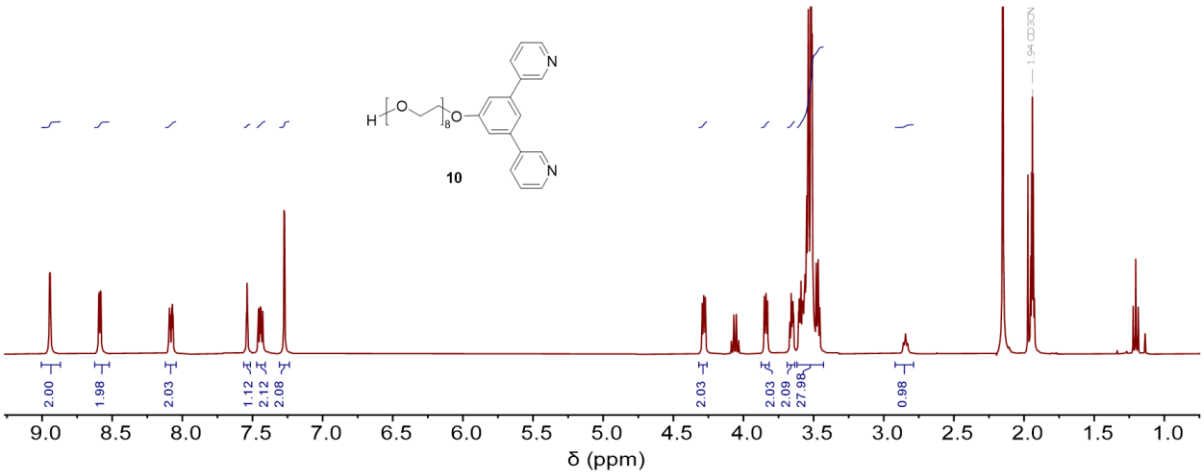


Figure S9. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **10**.

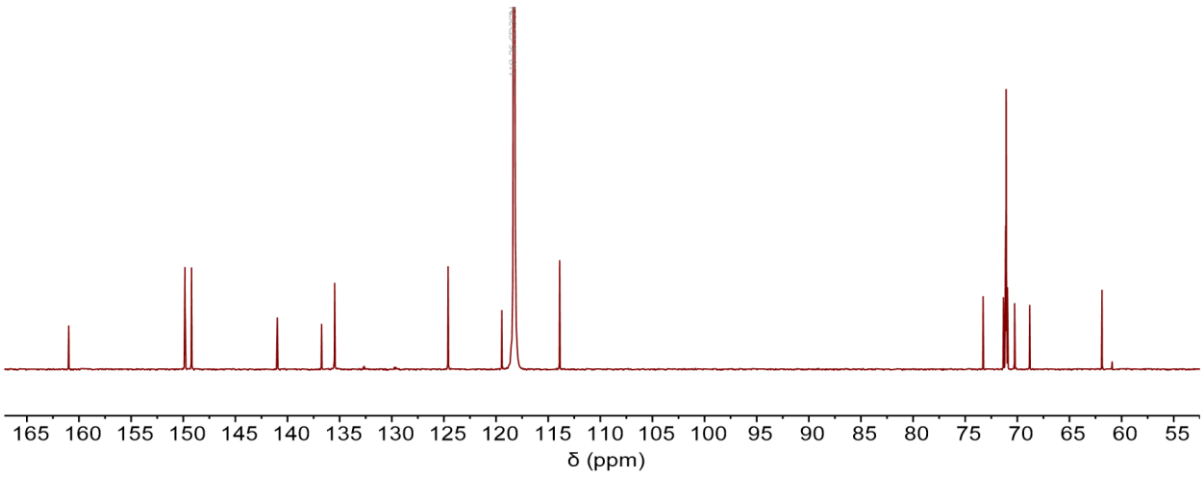


Figure S10. $^{13}C\{^1H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **10**.

Synthesis of compound 11

Compound **11** was synthesized following a similar procedure as used for compound **10**. Specifically, compound **7** (1.28 g, 1.0 equiv, 3.0 mmol), 4-pyridineboronic acid pinacol ester (**9**) (1.48 g, 2.4 equiv, 7.2 mmol), $Pd(PPh_3)_4$ (0.35 g, 0.1 equiv, 0.3 mmol), and K_2CO_3 (4.14 g, 10 equiv, 30 mmol) were added into a 50 mL single-neck round-bottom flask equipped with a magnetic stir bar and capped with a septum. Under a nitrogen atmosphere, DMF (20 mL) along with H_2O (1 mL) were added and the resulting mixture was stirred for 60 h at 100 °C. After cooling to room temperature, the mixture was diluted with chloroform/methanol (10/1, v/v) and filtered through Celite. The filtrate was washed with brine, dried over anhydrous magnesium sulfate, and purified by column chromatography (methanol: ethyl acetate, 1:3). Compound **11** was obtained as a colorless oil (1.32 g, 86%).

^{1}H NMR (400 MHz, CD_3CN) δ 8.70 – 8.59 (m, 4H), 7.71 – 7.63 (m, 4H), 7.60 (t, *J*=1.5, 1.5, 1H), 7.32 (d, *J*=1.5, 2H), 4.30 – 4.22 (m, 2H), 3.86 – 3.79 (m, 2H), 3.67 – 3.61 (m, 2H), 3.61 – 3.48 (m, 16H), 3.45 (dd, *J*=5.5, 4.1, 2H), 3.13 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, CD_3CN) δ 160.99, 151.16, 148.16, 141.15, 122.67, 119.13, 114.72, 73.30, 71.31, 71.10, 71.07, 71.05, 71.04, 70.92, 70.21, 68.86, 61.86. HRMS (ESI/QTOF) *m/z*: $[M + H]^+$ calcd. for $C_{28}H_{37}N_2O_7^+$ 513.2595, found 513.2606.

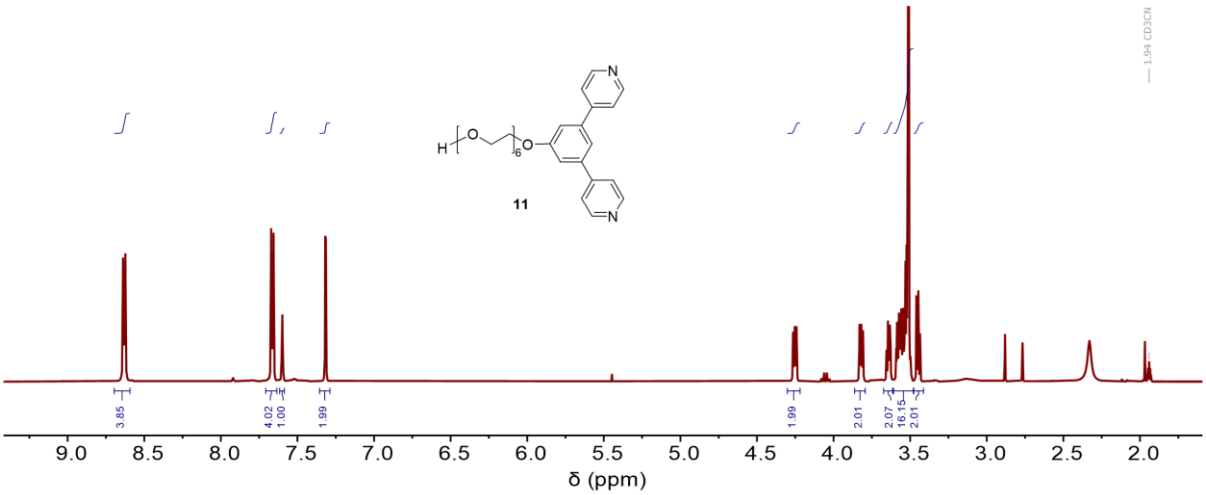


Figure S11. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **11**.

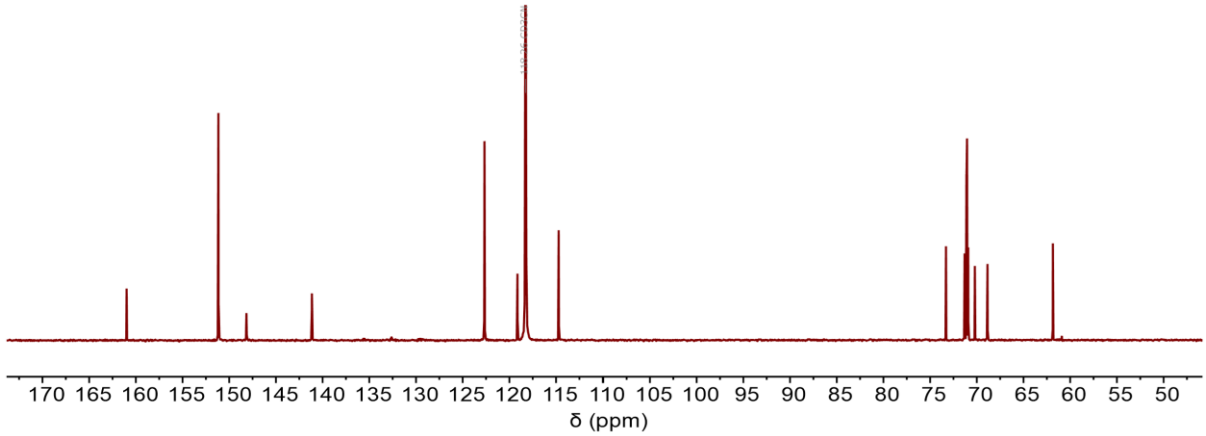


Figure S12. ^{13}C{^{1}H} NMR spectrum (101 MHz, CD_3CN) of compound **11**.

Synthesis of compounds L1 and L2

Compound **10** or **11** (1.0 equiv, 2.0 mmol) and triethylamine (1.15 mL, 4.0 equiv, 8.0 mmol) were dissolved in DCM (25 mL) and the resulting mixture was stirred at 0 °C for 1 h under a nitrogen atmosphere. Subsequently, acryloyl chloride (0.24 mL, 1.5 equiv, 3.0 mmol) was added. The solution was stirred at 0 °C for 3 h. After that, the solution was allowed to stand at room temperature for 36 h. The solution was then concentrated under vacuum and the residue was purified by chromatography on silica (**L1**: hexane: ethyl acetate, 1:20; **L2**: hexane: ethyl acetate, 1:30). Compound **L1** was obtained as a yellowish oil (1.14 g, 87%). Compound **L2** was obtained as a yellowish oil (1.03 g, 91%).

Compound L1: ^{1}H NMR (400 MHz, CD_3CN) δ 8.93 (dd, *J*=2.5, 0.9, 2H), 8.58 (dd, *J*=4.8, 1.6, 2H), 8.06 (ddd, *J*=7.9, 2.4, 1.6, 2H), 7.52 (t, *J*=1.5, 1.5, 1H), 7.43 (ddd, *J*=7.9, 4.8, 0.9, 2H), 7.25 (d, *J*=1.5, 2H), 6.34 (dd, *J*=17.3,

1.5, 1H), 6.13 (dd, *J*=17.3, 10.4, 1H), 5.85 (dd, *J*=10.4, 1.5, 1H), 4.28 – 4.24 (m, 2H), 4.24 – 4.20 (m, 2H), 3.86 – 3.79 (m, 2H), 3.67 – 3.62 (m, 4H), 3.61 – 3.47 (m, 22H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ 166.73, 160.96, 149.80, 149.17, 140.94, 136.70, 135.45, 131.60, 129.21, 124.59, 119.41, 113.87, 71.32, 71.12, 71.06, 71.05, 71.04, 71.00, 70.26, 69.54, 68.79, 64.52. HRMS (ESI/QTOF) *m*/*z*: $[M + H]^+$ calcd. for $C_{31}H_{39}N_2O_8^+$ 567.2701, found 567.2711.

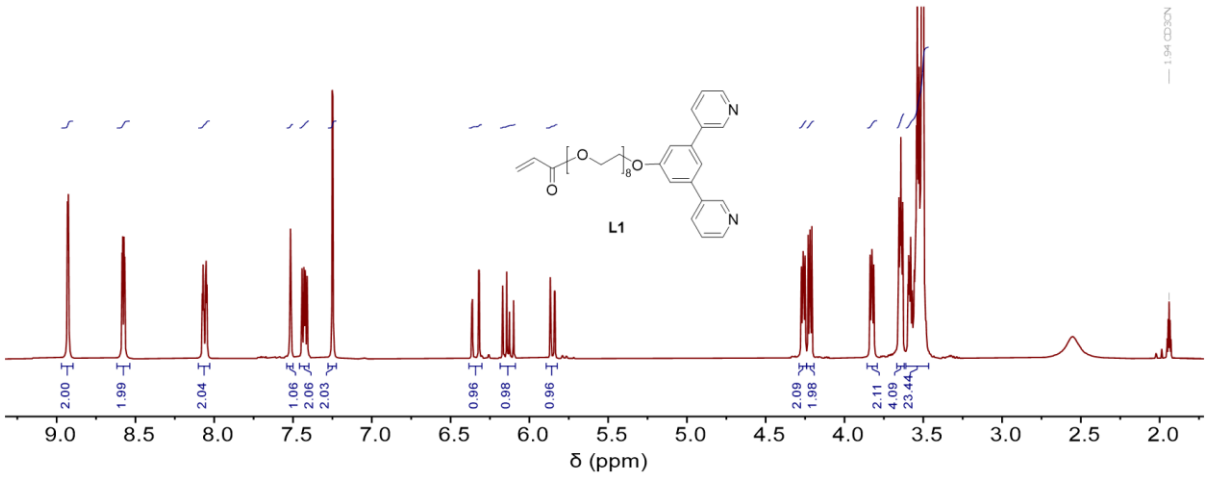


Figure S13. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **L1**.

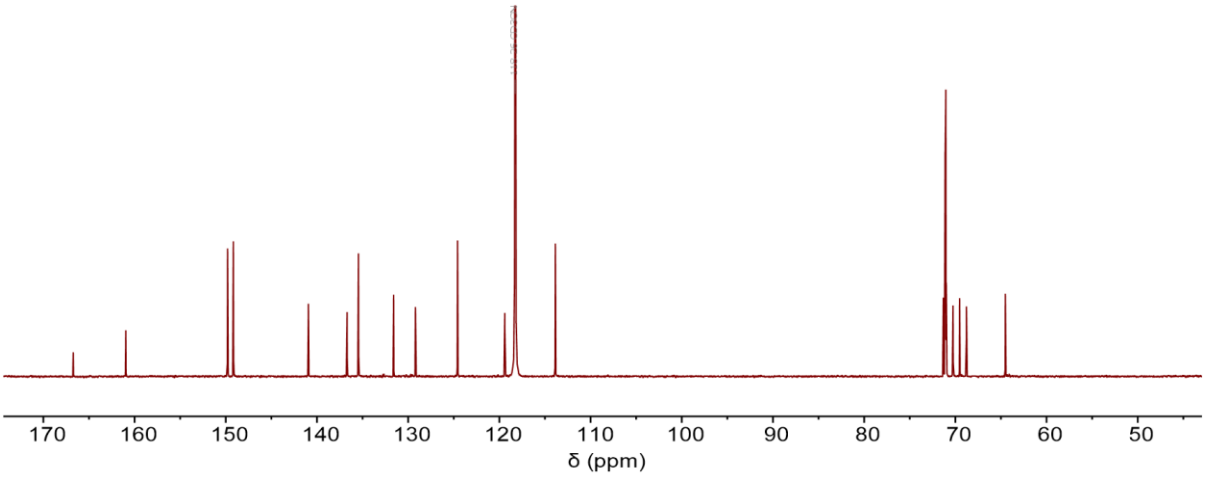


Figure S14. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **L1**.

Compound L2: ^{1}H NMR (400 MHz, CD_3CN) δ 8.68 – 8.62 (m, 4H), 7.73 – 7.68 (m, 4H), 7.64 (t, *J*=1.6, 1.6, 1H), 7.36 (d, *J*=1.5, 2H), 6.34 (dd, *J*=17.3, 1.6, 1H), 6.13 (dd, *J*=17.3, 10.4, 1H), 5.85 (dd, *J*=10.4, 1.5, 1H), 4.32 – 4.26 (m, 2H), 4.24 – 4.19 (m, 2H), 3.87 – 3.82 (m, 2H), 3.68 – 3.61 (m, 4H), 3.61 – 3.57 (m, 2H), 3.57 – 3.49 (m, 12H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3CN) δ 166.75, 161.07, 151.23, 148.19, 141.31, 131.58, 129.22, 122.71, 119.23, 118.26, 114.77, 71.35, 71.14, 71.13, 71.11, 71.09, 71.07, 71.01, 70.25, 69.55, 68.93, 64.53. HRMS (APCI/QTOF) *m*/*z*: $[M + Na]^+$ calcd. for $C_{35}H_{46}N_2NaO_{10}^+$ 677.3045, found 677.3039.

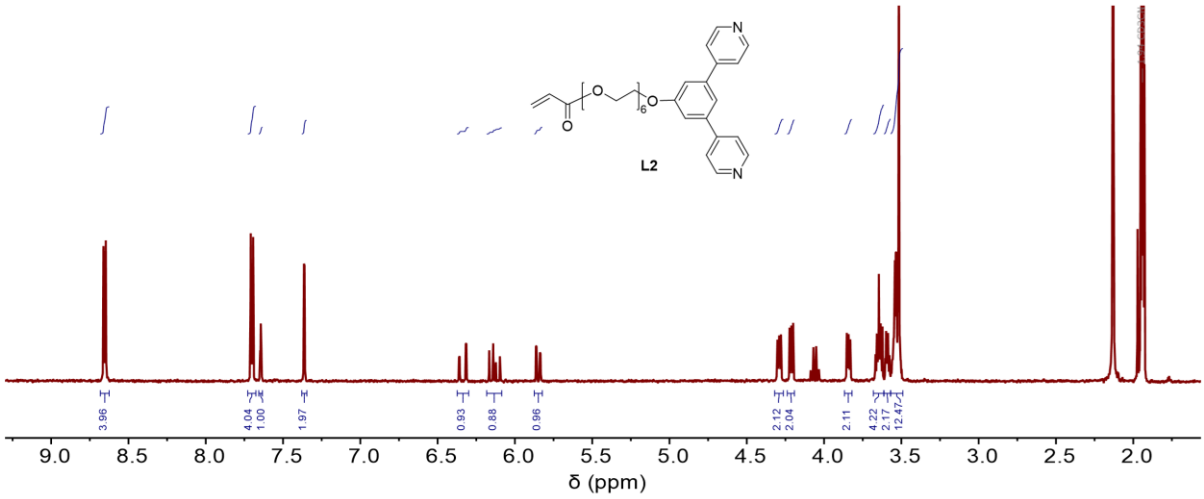


Figure S15. ^{1}H NMR spectrum (400 MHz, CD_3CN) of compound **L2.**

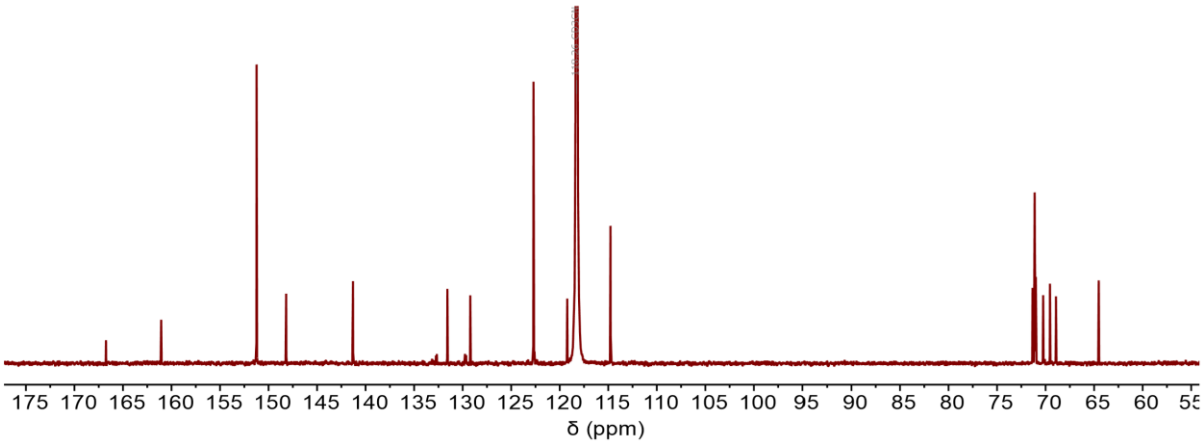
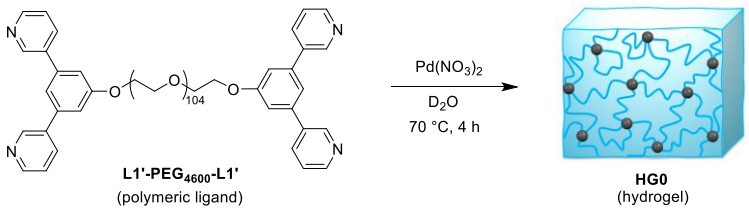


Figure S16. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of compound **L2**.

2.2 Synthesis of hydrogel HG0 by Pd^{2+}-mediated crosslinking of a polymeric ligand

The hydrogel **HG0** was synthesized according to a modified literature procedure.[1] Specifically, 20 mg of the polymeric ligand **L1'-PEG$_{4600}$-L1'** was dissolved in 460 μL of D_2O. Subsequently,40 μL of a 100 mM $Pd(NO_3)_2$ stock solution in D_2O was added. The mixture was vortexed till they were mixed well before it was annealed at 70 °C for 4 h to obtain hydrogel **HG0**.



Scheme S3. Synthesis of supramolecular hydrogel **HG0**.

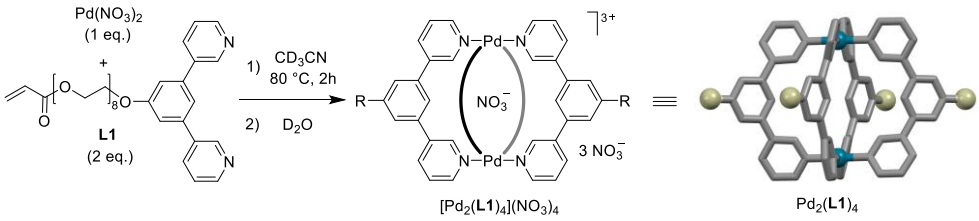
HG0

Figure S17. Picture of the supramolecular hydrogel **HG0**. The strong coloration indicates partial decomposition of the Pd complexes.

2.3 Synthesis and characterization of cage $[Pd_2(L1)_4](NO_3)_4$

Cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$ was synthesized by stirring a mixture of ligand **L1** (50 µmol, 1000 µL of a 50 mM stock solution of **L1** in CD_3CN) and $Pd(NO_3)_2$ (25 µmol, 500 µL of a 50 mM stock solution in CD_3CN) in CD_3CN (1000 µL) at 80 °C for 2 h to give 2500 µL of a 5 mM solution of $[Pd_2(\mathbf{L1})_4](NO_3)_4$. The cage was characterized by NMR spectroscopy and mass spectrometry. Subsequently, the solvent was removed under reduced pressure and the residue was dissolved in D_2O (2500 µL) to give a 5 mM solution of $[Pd_2(\mathbf{L1})_4](NO_3)_4$. The structural integrity of the cage after solvent exchange was verified by ^{1}H NMR spectroscopy.

^{1}H NMR (400 MHz, CD_3CN) δ 10.26 (d, *J*=2.0, 2H), 9.49 (dd, *J*=5.8, 1.3, 2H), 8.79 (t, *J*=1.6, 1.6, 1H), 8.30 (dt, *J*=8.3, 1.6, 1.6, 2H), 7.66 (dd, *J*=8.1, 5.7, 2H), 7.24 (d, *J*=1.5, 2H), 6.28 (dd, *J*=17.3, 1.5, 1H), 6.07 (dd, *J*=17.3, 10.4, 1H), 5.80 (dd, *J*=10.4, 1.5, 1H), 4.19 – 4.10 (m, 4H), 3.76 – 3.69 (m, 2H), 3.60 – 3.54 (m, 4H), 3.51 – 3.39 (m, 22H). ^{13}C{^{1}H} NMR (126 MHz, CD_3CN) δ 166.66, 161.48, 151.49, 151.35, 139.96, 139.41, 138.02, 131.58, 129.14, 128.16, 120.18, 114.98, 71.25, 71.08, 71.04, 71.02, 70.99, 70.98, 70.96, 70.07, 69.50, 68.99, 64.47. HRMS (APCI/QTOF) *m/z*: [M - 3(NO_3)]$^{3+}$ calcd. for $Pd_2C_{140}H_{184}N_9O_{43}^{3+}$ most abundant 964.35412, found 964.35407.



Scheme S4. Synthesis of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

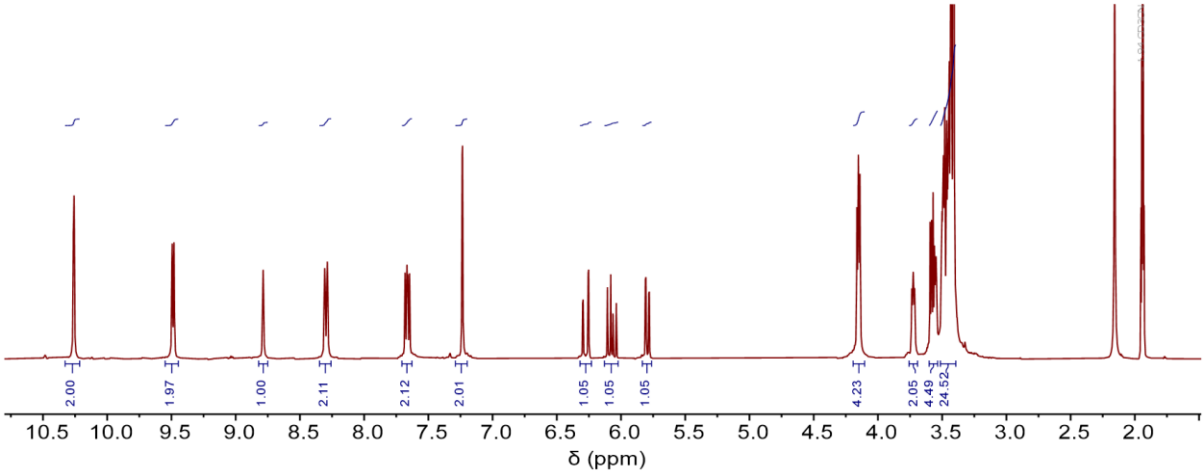


Figure S18. ^{1}H NMR spectrum (400 MHz, CD_3CN) of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

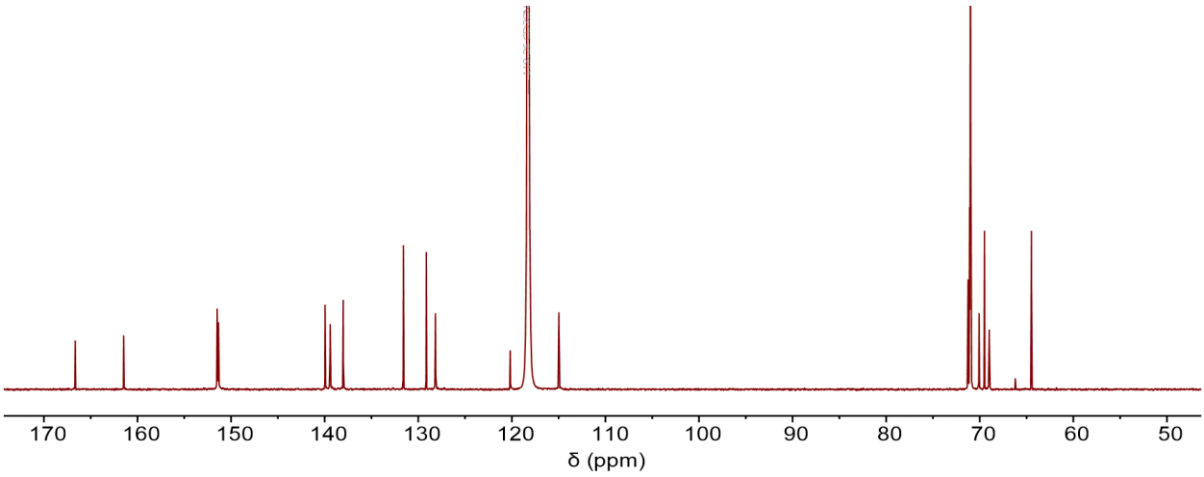


Figure S19. $^{13}C\{^{1}H\}$ NMR spectrum (101 MHz, CD_3CN) of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

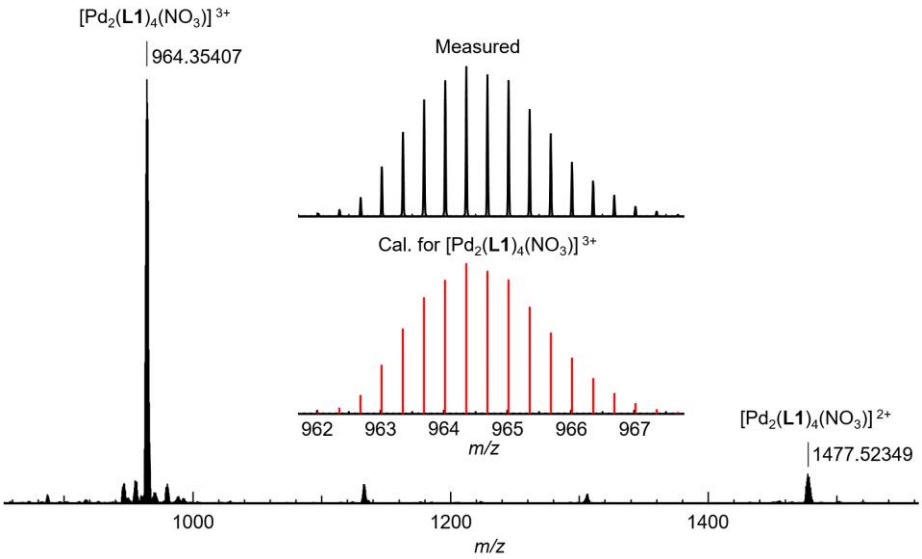


Figure S20. High-resolution ESI-MS spectrum of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

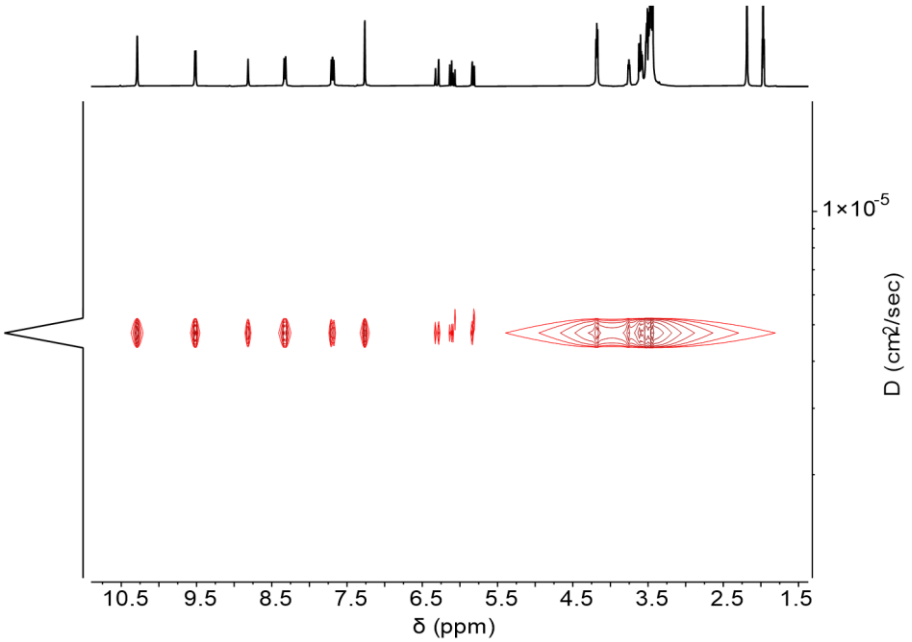


Figure S21. DOSY NMR spectrum of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

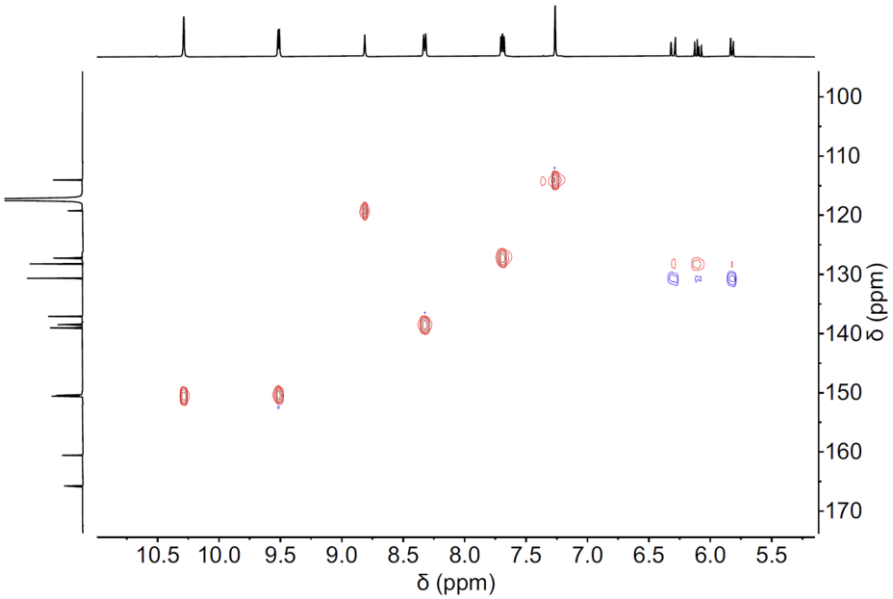


Figure S22. HSQC NMR spectrum of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

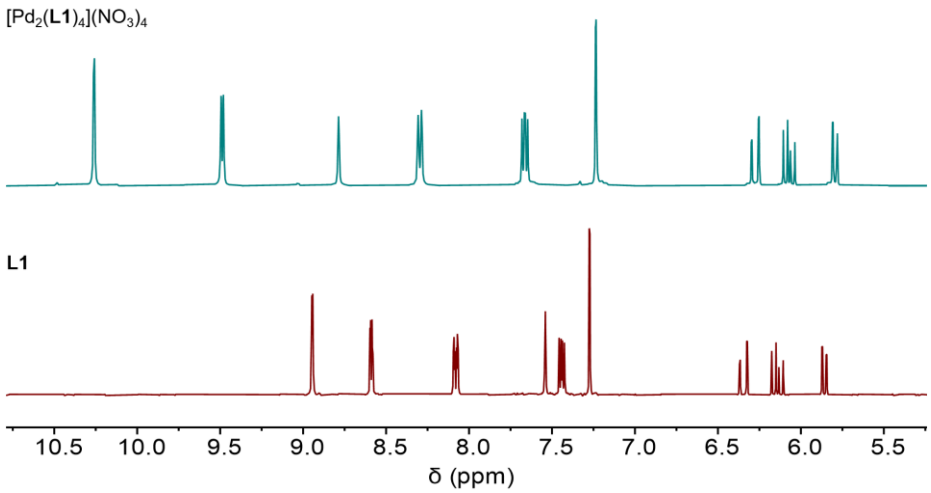


Figure S23. ^{1}H NMR spectrum (400 MHz, CD_3CN) of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$ and **L1**.

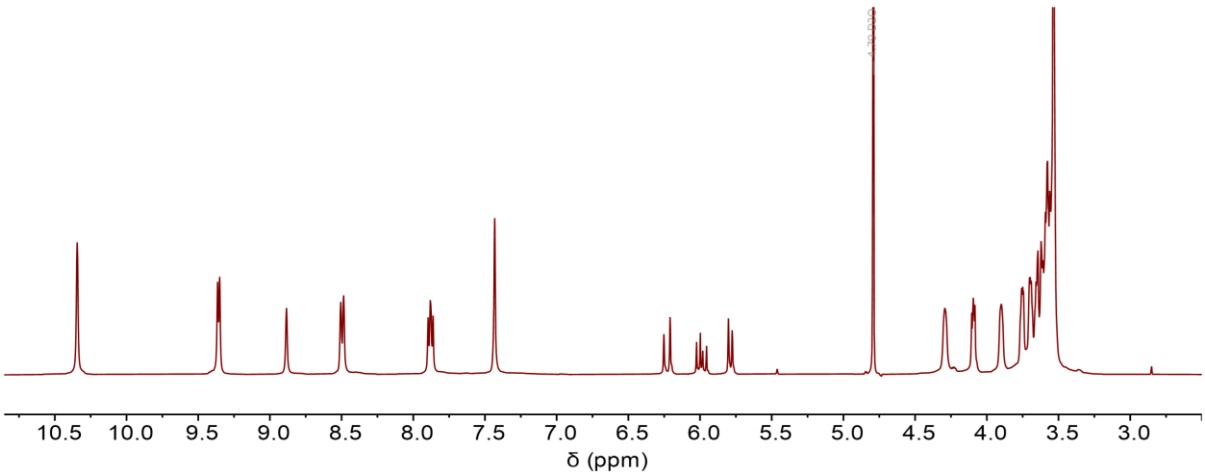
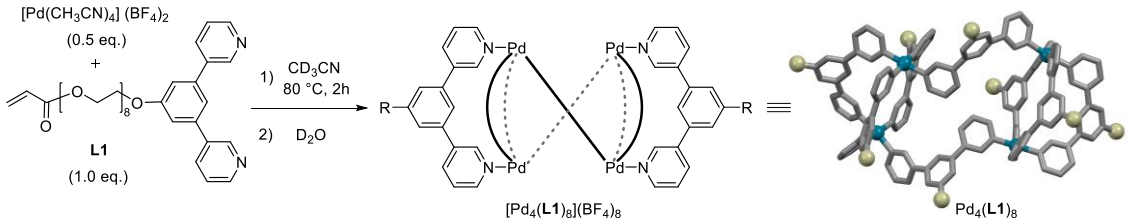


Figure S24. ^{1}H NMR spectrum (400 MHz, D_2O) of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$.

2.4 Synthesis and characterization of cage $[Pd_4(L1)_8]$ $(BF_4)_8$

Cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$ was synthesized by stirring a mixture of ligand **L1** (25 µmol, 500 µL of a 50 mM stock solution of **L1** in CD_3CN) and $[Pd(CH_3CN)_4](BF_4)_2$ (12.5 µmol, 250 µL of a 50 mM stock solution in CD_3CN) in CD_3CN (500 µL) at 80 °C for 2 h. Subsequently, the solvent was removed under reduced pressure and the residue was dissolved in D_2O (1250 µL) to give a 2.5 mM solution of $[Pd_2(\mathbf{L1})_8]$ $(BF_4)_8$. ^{1}H NMR (500 MHz, D_2O) δ 10.45 (s, 1H), 10.20 (s, 1H), 9.84 (dd, *J* = 10.2, 5.7 Hz, 3H), 9.69 (s, 1H), 9.49 (d, *J* = 24.2 Hz, 3H), 9.29 – 9.16 (m, 3H), 9.10 (d, *J* = 5.5 Hz, 1H), 8.70 (d, *J* = 5.5 Hz, 1H), 8.61 (d, *J* = 8.1 Hz, 1H), 8.53 (d, *J* = 8.3 Hz, 1H), 8.41 (dd, *J* = 21.6, 8.2 Hz, 3H), 8.30 (d, *J* = 8.1 Hz, 1H), 8.23 (s, 1H), 8.18 (dd, *J* = 11.5, 7.0 Hz, 2H), 8.11 (s, 1H), 7.98 (p, *J* = 5.9 Hz, 3H), 7.87 (s, 1H), 7.86 – 7.79 (m, 2H), 7.78 – 7.70 (m, 3H), 7.66 (s, 1H), 7.62 – 7.56 (m, 1H), 7.42 (s, 1H), 7.40 (s, 1H), 7.33 (s, 2H), 7.28 (s, 1H), 6.94 (s, 1H), 6.89 (s, 1H), 6.49 (s, 1H), 6.12 – 5.98 (m, 5H), 5.93 – 5.78 (m, 4H), 5.72 – 5.57 (m, 4H), 4.40 (s, 2H), 4.24 (d, *J* = 7.7 Hz, 5H), 4.04 (s, 3H), 4.00 – 3.93 (m, 7H), 3.92 – 3.81 (m, 10H), 3.76 (t, *J* = 4.4 Hz, 3H), 3.73 – 3.32 (m, 127H), 3.02 (d, *J* = 31.5 Hz, 2H), 2.91 – 2.76 (m, 2H). HRMS (APCI/QTOF) *m/z*: $[M - 3(NO_3)]^{3+}$ calcd. for $Pd_4C_{280}H_{368}N_{16}O_{80}B_3F_{12}^{5+}$ most abundant 1184.62928, found 1184.62919.



Scheme S5. Synthesis of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$.

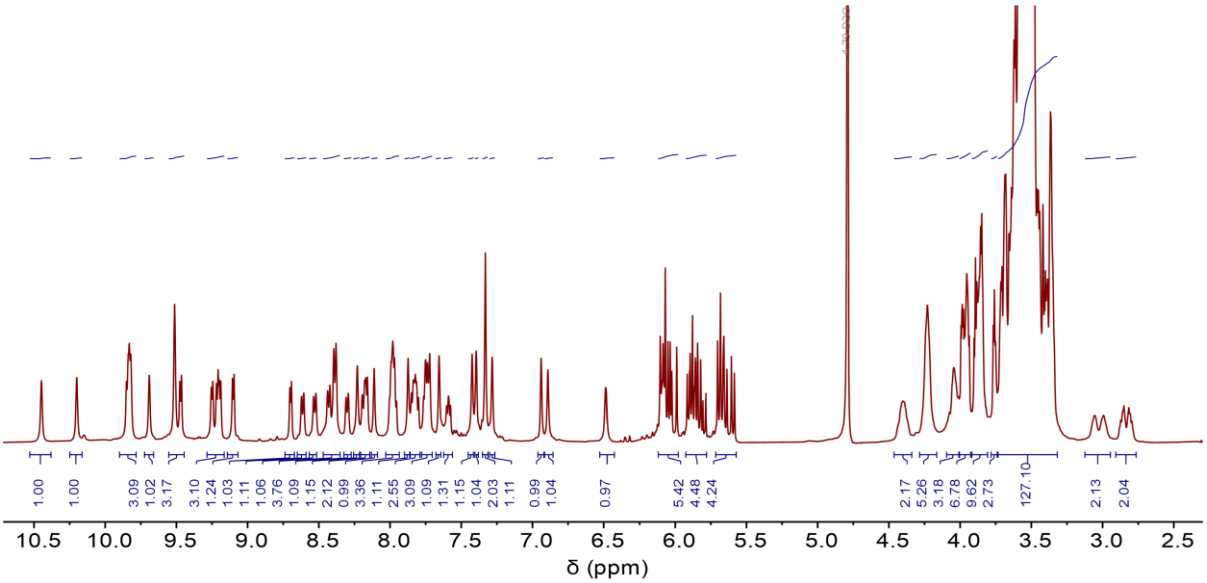


Figure S25. ^{1}H NMR spectrum (500 MHz, D_2O) of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$.

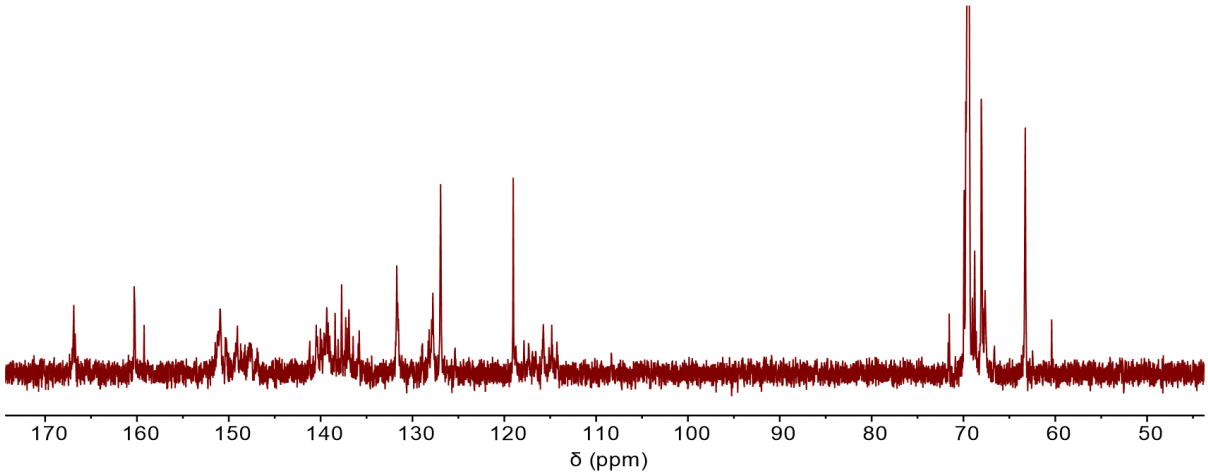


Figure S26. $^{13}C\{^{1}H\}$ NMR spectrum (151 MHz, D_2O) of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$. The poor quality of the spectrum is related to the low apparent symmetry of the cage and its limited solubility in D_2O.

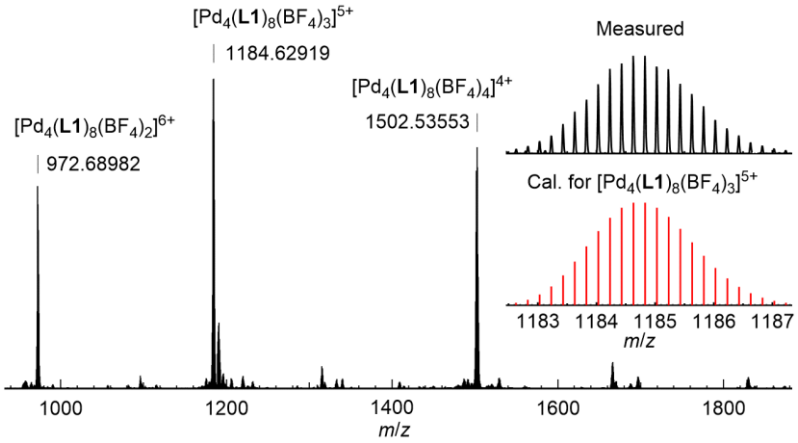


Figure S27. High-resolution ESI-MS spectrum of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$.

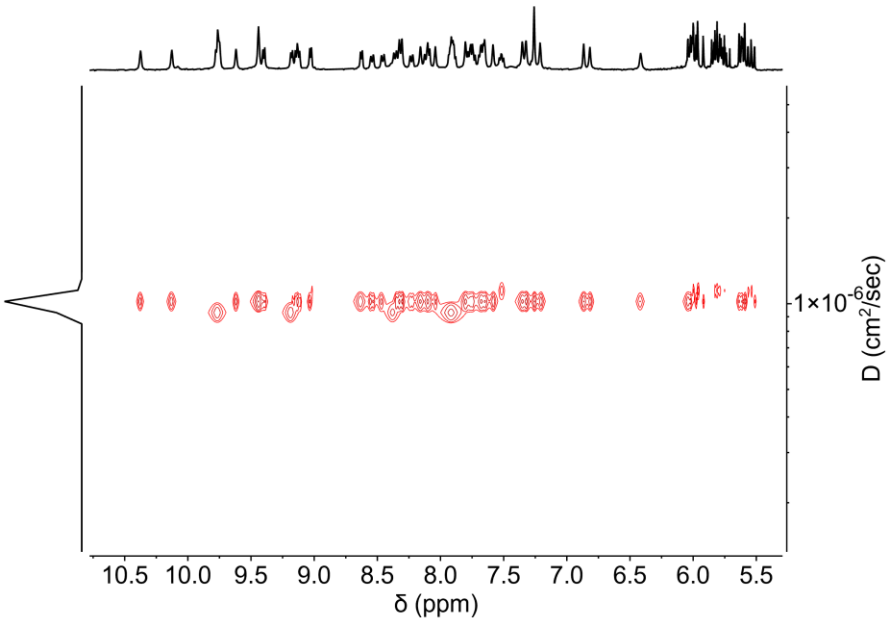


Figure S28. DOSY NMR spectrum of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$.

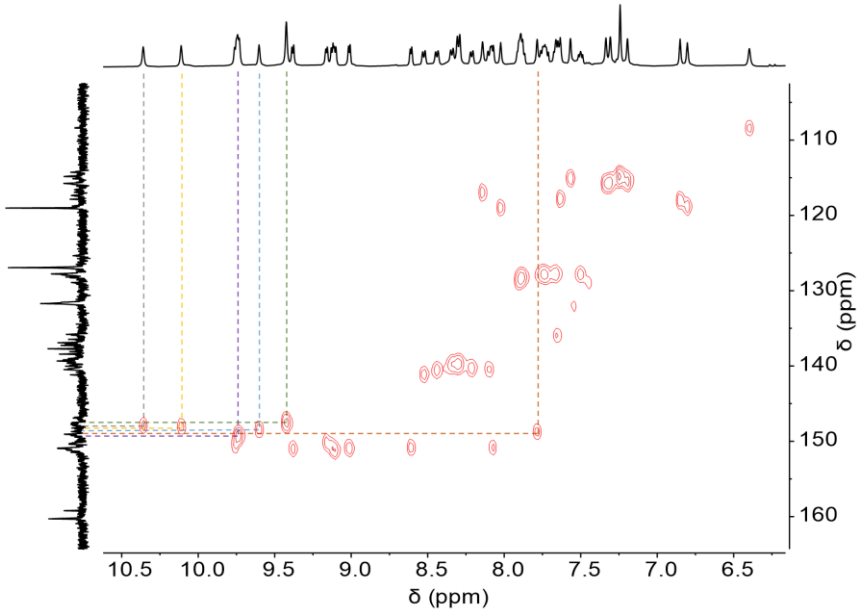


Figure S29. HSQC NMR spectrum of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$.

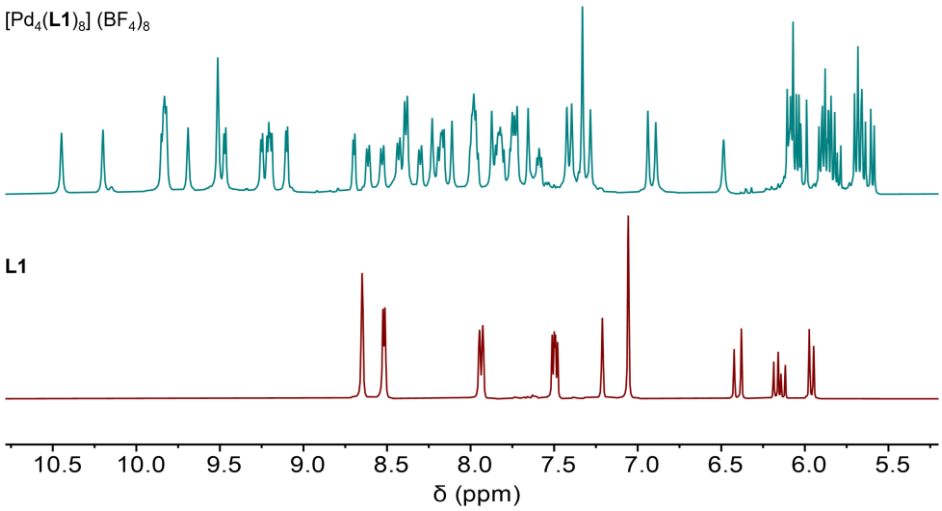
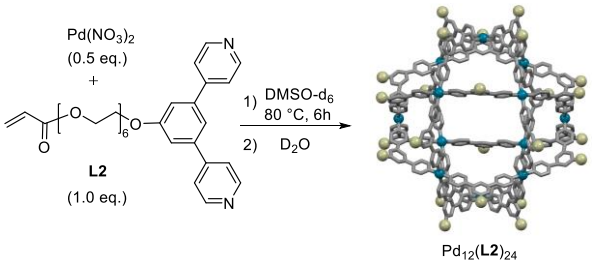


Figure S30. ^{1}H NMR spectrum (400 MHz, D_2O) of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$ and **L1**.

2.5 Synthesis and characterization of cage $[Pd_{12}(L2)_{24}](NO_3)_{24}$

Cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$ was synthesized by stirring a mixture of ligand **L2** (25 µmol, 500 µL of a 50 mM stock solution of **L2** in DMSO-d_6) and $Pd(NO_3)_2$ (12.5 µmol, 250 µL of a 50 mM stock solution in DMSO-d_6) in DMSO-d_6 (500 µL) at 80 °C for 6 h to give 1250 µL of a 0.83 mM solution of $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$. The cage was characterized by NMR spectroscopy. Attempts to obtain a mass spectrum of the cage were not successful. Subsequently, the solution was diluted five times with D_2O and then lyophilized. The residue was dissolved in D_2O (1250 µL) to give 1250 µL of a 0.83 mM solution of $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.64 – 9.38 (m, 4H), 8.30 (d, J = 5.9 Hz, 4H), 8.02 (s, 1H), 7.55 (s, 2H), 6.20 (dd, J = 17.3, 1.6 Hz, 1H), 6.02 (dd, J = 17.3, 10.3 Hz, 1H), 5.76 (dd, J = 10.4, 1.6 Hz, 1H), 4.22 (s, 2H), 4.18 – 3.98 (m, 2H), 3.75 (s, 2H), 3.69 – 3.31

(m, 18H).$^{13}C\{^{1}H\}$ NMR (151 MHz, DMSO) δ 171.51, 165.31, 159.96, 151.05, 149.16, 136.30, 131.48, 128.02, 124.39, 118.28, 115.38, 69.89, 69.76, 69.72, 69.69, 69.66, 69.63, 68.77, 68.11, 67.76, 63.31.



Scheme S6. Synthesis of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$.

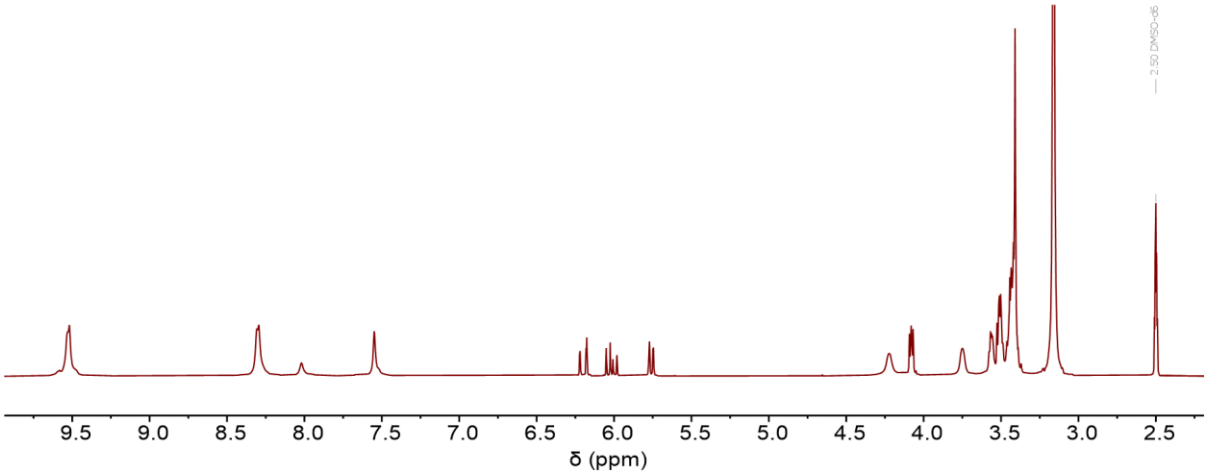


Figure S31. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$.

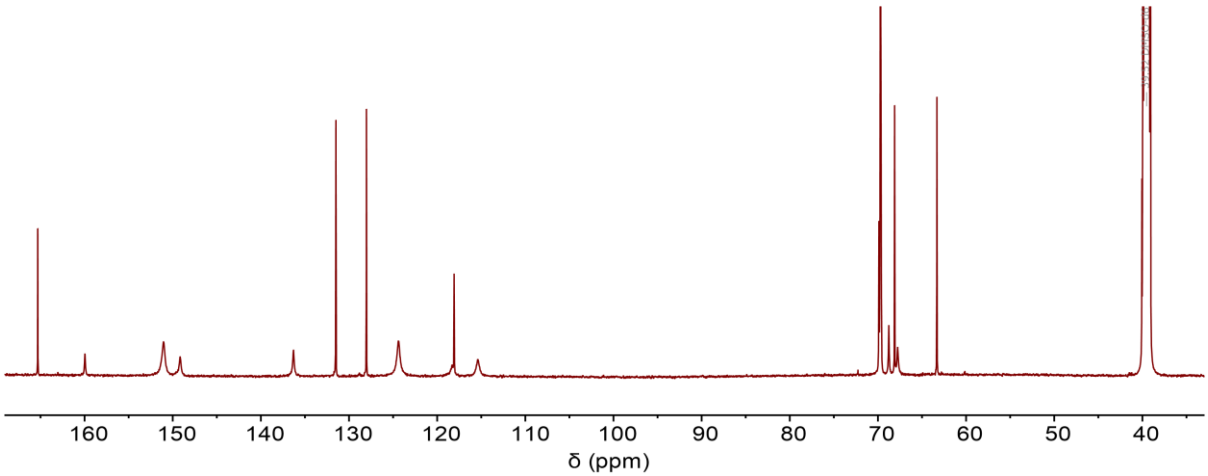


Figure S32. $^{13}C\{^{1}H\}$ NMR spectrum (151 MHz, DMSO-d_6) of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$.

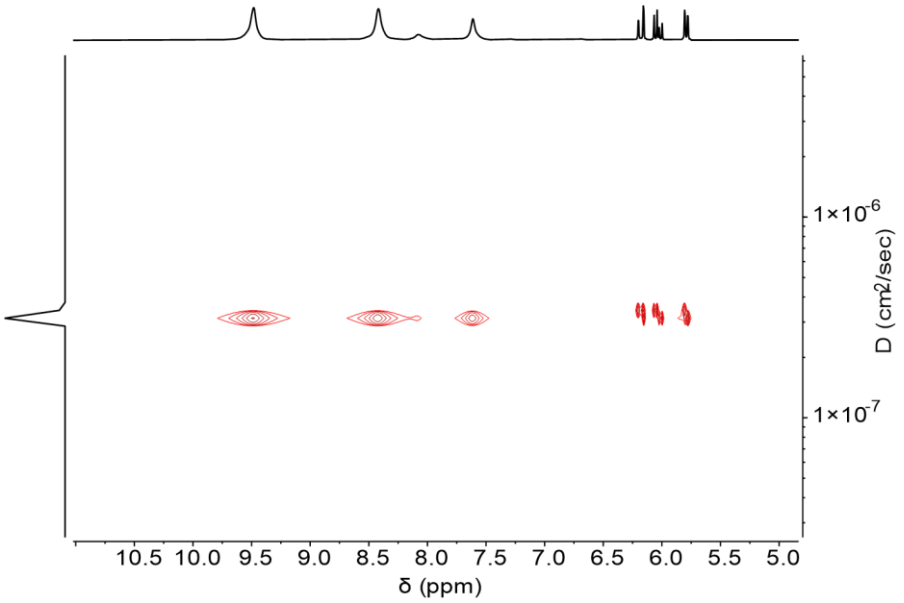


Figure S33. DOSY NMR spectrum of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$.

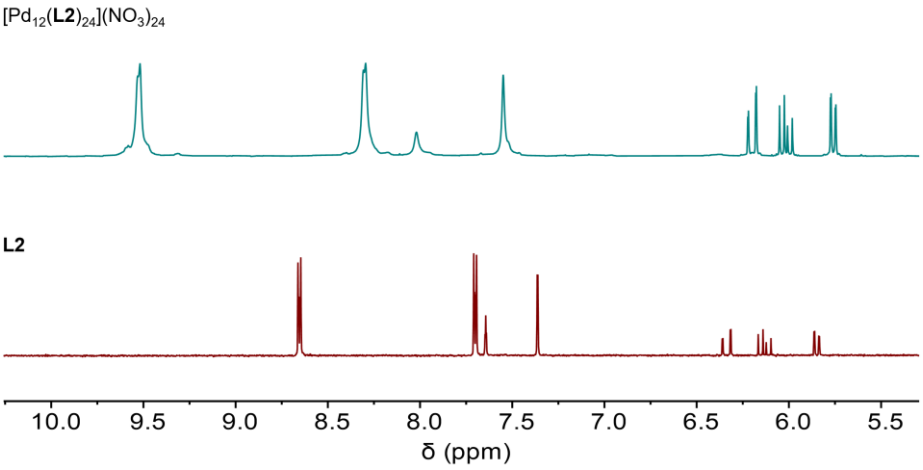


Figure S34. ^{1}H NMR spectrum (400 MHz, DMSO-d_6) of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$ and **L2**.

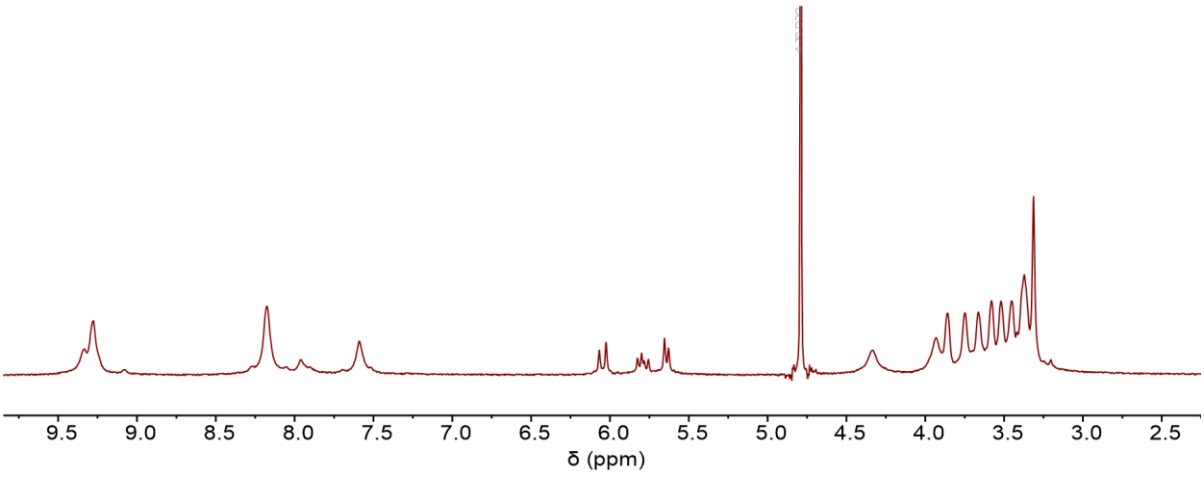
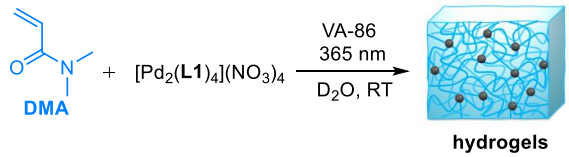


Figure S35. ^{1}H NMR spectrum (400 MHz, D_2O) of cage $[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$.

2.6 Synthesis and characterization of the hydrogels HG1–HG3

The cage-crosslinked hydrogels **HG1**–**HG3** were synthesized via photoinitiated radical copolymerization. Specifically, monomer DMA (19.83 mg, 200 μmol), initiator VA-86 (3.0 μmol, 1.5 mol%) and different amounts of cage $[Pd_2(\mathbf{L1})_4](NO_3)_4$ (1.25 mol%, 0.63 mol%, or 0.31 mol%,) were dissolved in D_2O (500 μL) in a 1.5 mL glass vial. The mixture was purged with N_2 for 30 min, then irradiated by a UV lamp for 1 h. After 12 h of incubating at RT, stable hydrogels were obtained. The hydrogels were characterized by ^1H NMR spectroscopy. The mechanical properties of the hydrogels were examined by rheometry. The swelling capability of the hydrogels was examined as described in section 1.2.



Scheme S7. Synthesis of the cage-crosslinked hydrogels **HG1**, **HG2**, and **HG3**.

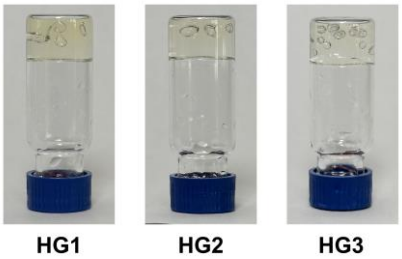


Figure S36. Pictures of the cage-crosslinked hydrogels **HG1**, **HG2**, and **HG3**.

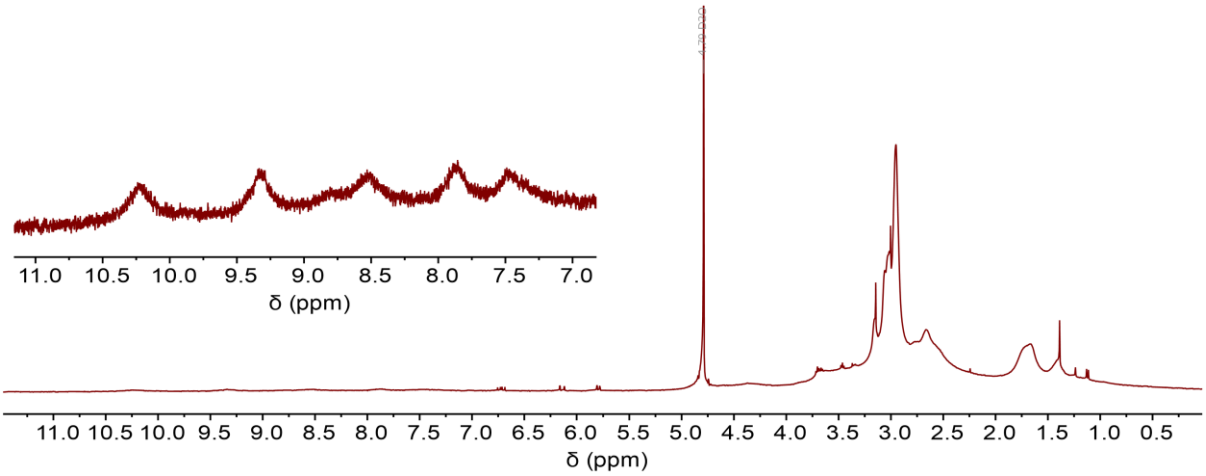


Figure S37. ^1H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG1**.

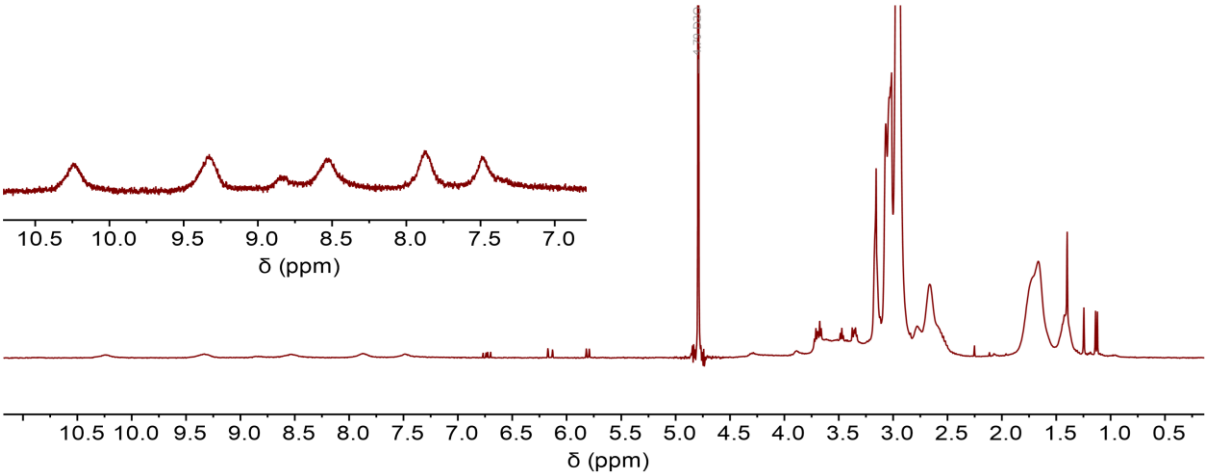


Figure S38. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG2**.

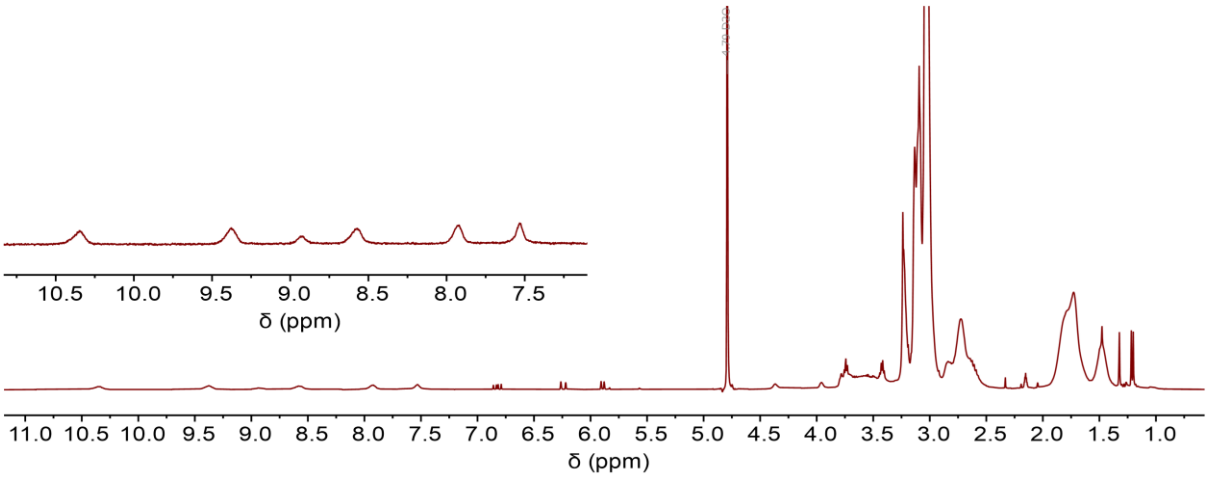


Figure S39. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG3**.

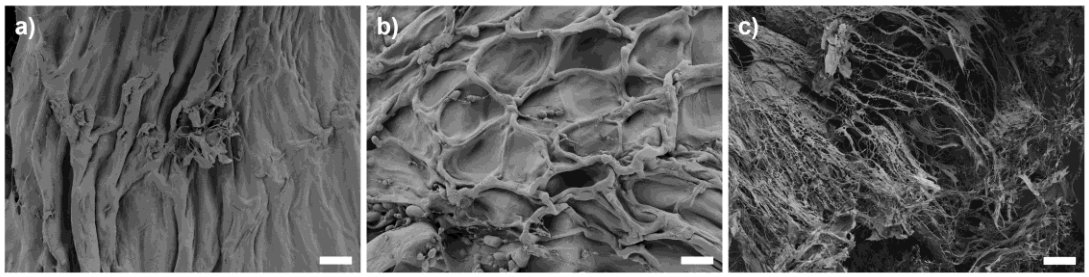


Figure S40. SEM images of **HG1** (**a**), **HG2** (**b**), and **HG3** (**c**), scale bar 50 μm.

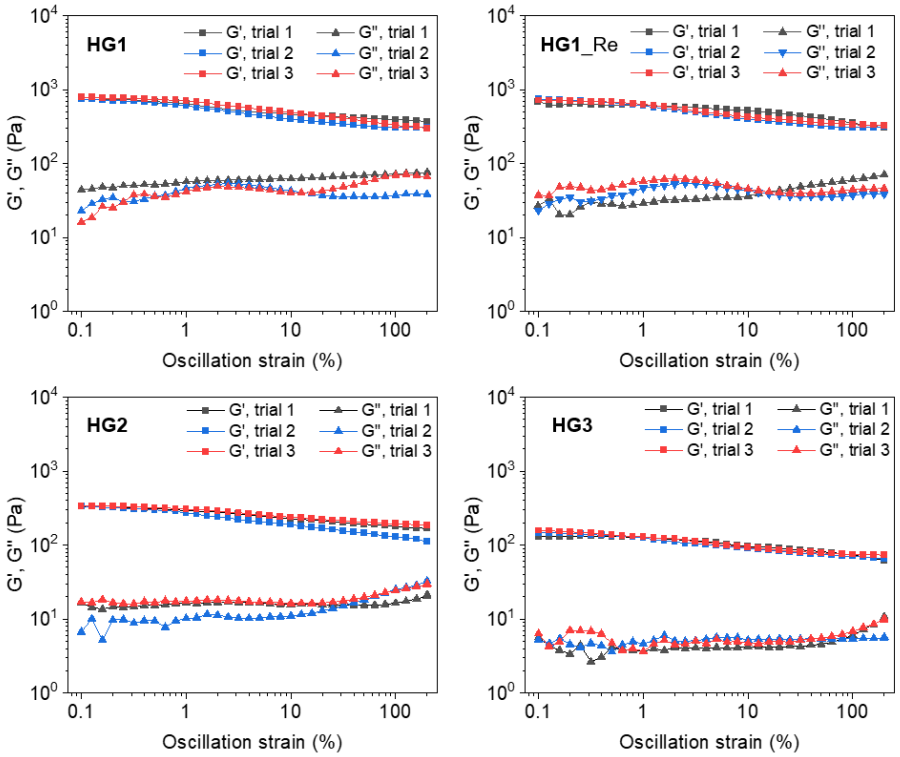


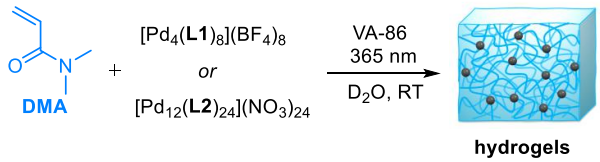
Figure S41. Amplitude sweeps in oscillatory rheology from 0.1% to 200% strain at frequency of 1 rad s^{-1} for **HG1**–**HG3** at 25 °C. The gel **HG1** was re-measured after standing at RT for one week (**HG1**_Re).

Table S1. Synthesis and characterization of **HG1**, **HG2**, and **HG3**.

	Monomer	Cage-crosslinker	Storage moduli (G')	Swelling capacities
HG1	DMA (200 μmol)	$[Pd_2(\mathbf{L1})_4](NO_3)_4$ (2.50 μmol)	742.8 Pa	42
HG2	DMA (200 μmol)	$[Pd_2(\mathbf{L1})_4](NO_3)_4$ (1.25 μmol)	331.9 Pa	35
HG3	DMA (200 μmol)	$[Pd_2(\mathbf{L1})_4](NO_3)_4$ (0.63 μmol)	129.7 Pa	31

2.7 Synthesis and characterization of hydrogels HG4 and HG5

For the synthesis of **HG4**, DMA (200 µmol) was used as monomer and cage $[Pd_4(\mathbf{L1})_8]$ $(BF_4)_8$ (1.25 µmol, 0.63 mol%) was used as crosslinker. For the synthesis of **HG5**, DMA (200 µmol) was used as monomer and cage $Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$ (0.42 µmol, 0.21 mol%) was used as crosslinker. The polymerization was carried out as described for **HG1**–**HG3**. The hydrogels were characterized by ^{1}H NMR spectroscopy. The mechanical properties of the hydrogels were examined by rheometry. The swelling capability of the hydrogels was examined as described in section 1.2.



Scheme S8. Synthesis of the cage-crosslinked hydrogels **HG4** and **HG5**.

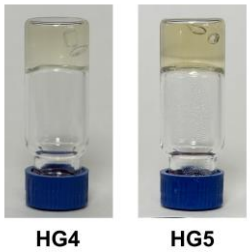


Figure S42. Pictures of cage-crosslinked hydrogels **HG4** and **HG5**.

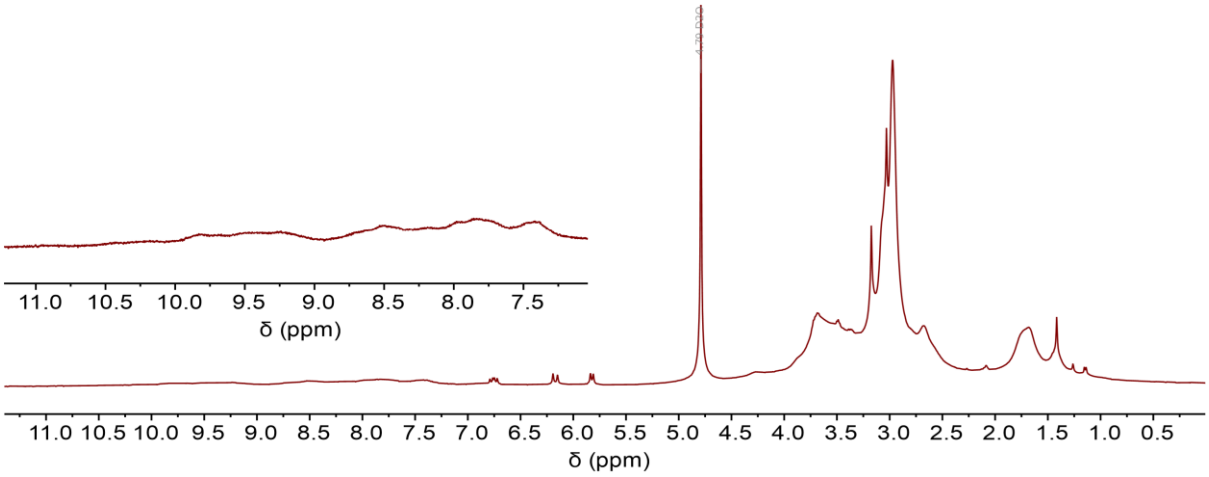


Figure S43. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG4**.

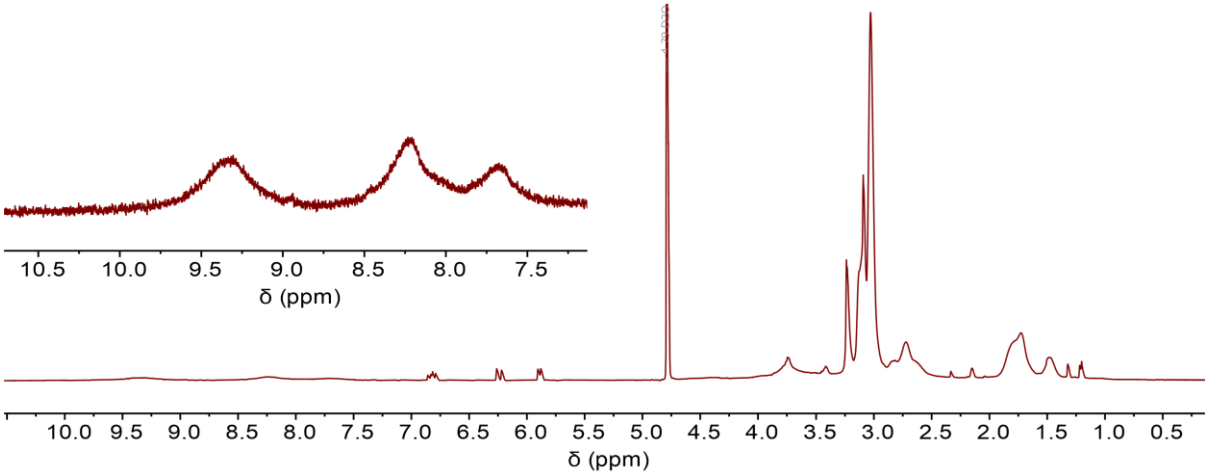


Figure S44. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG5**.

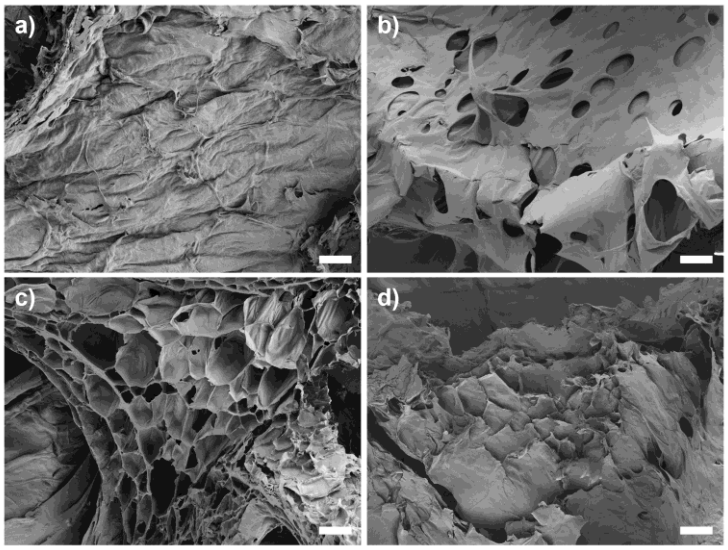


Figure S45. SEM images of **HG4** (**a**, **c**) and **HG5** (**b**, **d**), scale bar 50 μm.

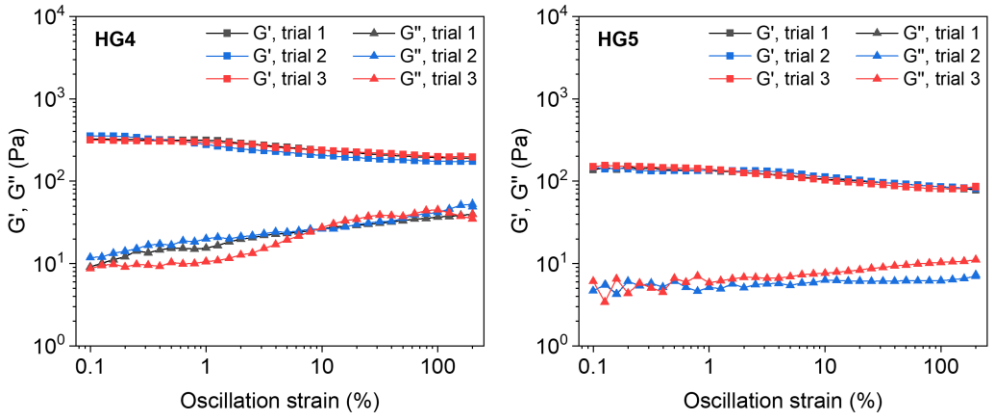


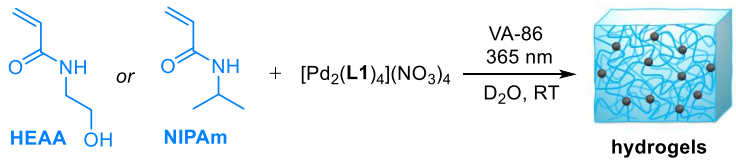
Figure S46. Amplitude sweeps in oscillatory rheology from 0.1% to 200% strain at frequency of 1 rad s^{-1} for **HG4** and **HG5** at 25 °C.

Table S2. Synthesis and characterization of **HG4** and **HG5**.

	Monomer	Cage-crosslinker	Storage moduli (G')	Swelling capacities
HG4	DMA (200 μmol)	$[Pd_4(\mathbf{L1})_8]$ $(BF_4)_8$ (1.25 μmol)	325.9 Pa	34
HG5	DMA (200 μmol)	$[Pd_{12}(\mathbf{L2})_{24}](NO_3)_{24}$ (0.42 μmol)	136.4 Pa	36

2.8 Synthesis and characterization of the hydrogels HG6 and HG7

For the synthesis of **HG6** and **HG7**, cage $Pd_2(\mathbf{L1})_4](NO_3)_4$ (2.50 μmol, 1.25 mol%) was used as crosslinker, while HEAA (200 μmol) and NIPAm (200 μmol) were used as monomers, respectively. The polymerization was carried out as described for **HG1**–**HG3**. The hydrogels were characterized by ^{1}H NMR spectroscopy. The mechanical properties of the hydrogels were examined by rheometry. The swelling capability of the hydrogels was examined as described in section 1.2.



Scheme S9. Synthesis of the cage-crosslinked hydrogels **HG6** and **HG7**.

Figure S47. Pictures of cage-crosslinked hydrogels **HG6** and **HG7**.

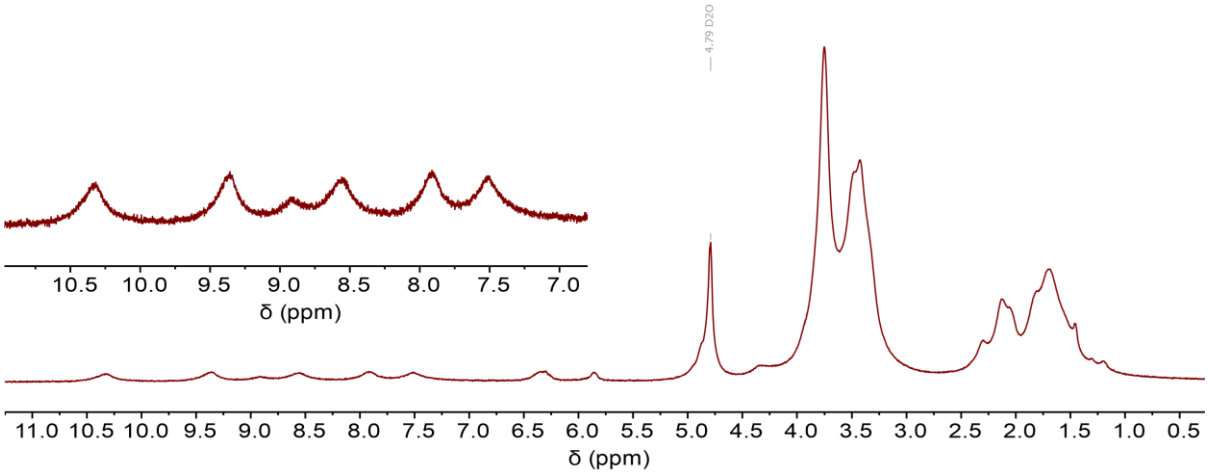


Figure S48. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG6**.

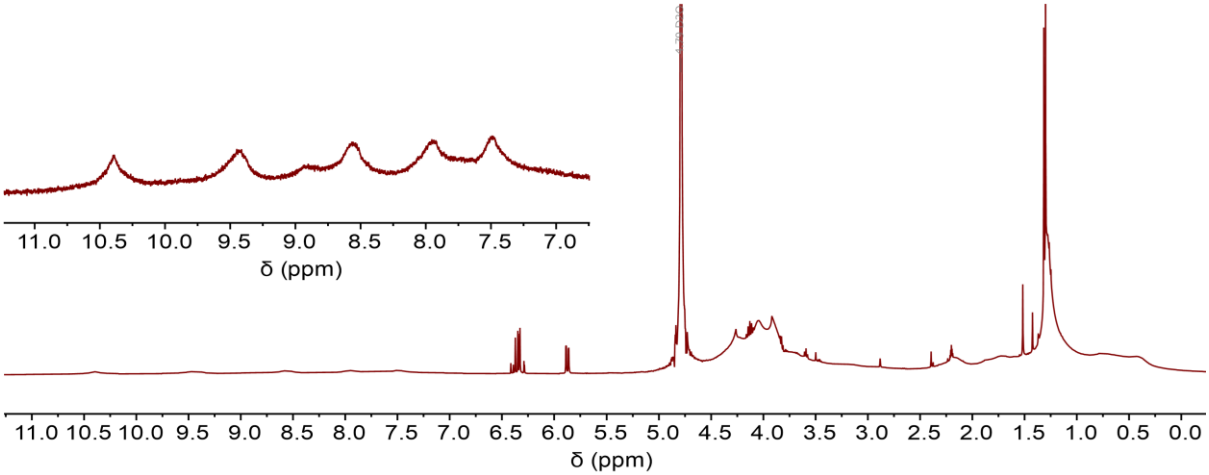


Figure S49. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogel **HG7**.

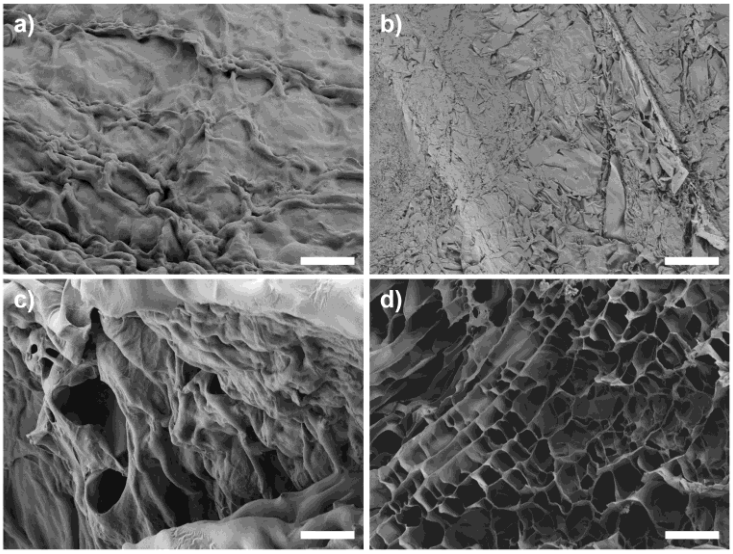


Figure S50. SEM images of **HG6** (**a**, **c**) and **HG7** (**b**, **d**), scale bar 40 μm.

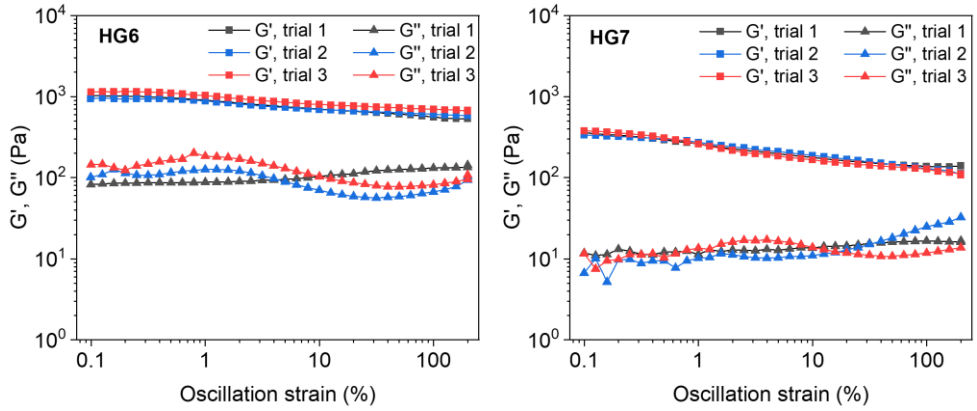


Figure S51. Amplitude sweeps in oscillatory rheology from 0.1% to 200% strain at frequency of 1 rad s^{-1} for **HG6** and **HG7** at 25 °C.

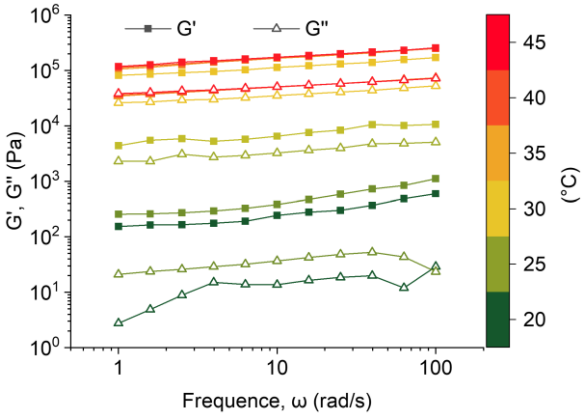


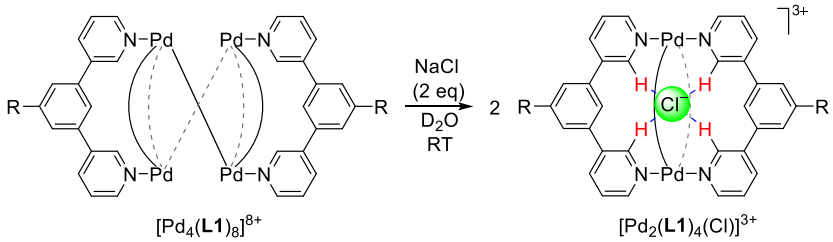
Figure S52. Frequency sweeps in oscillatory rheology from 1 to 100 rad s^{-1} at 1.0 % strain amplitude for **HG7** at different temperatures.

Table S3. Synthesis and characterization of **HG6** and **HG7**.

	Monomer	Cage-crosslinker	Storage moduli (G')	Swelling capacities
HG6	HEAA (200 µmol)	$[Pd_2(\mathbf{L1})_4](NO_3)_4$ (2.50 µmol)	1021.8 Pa	25
HG7	NIPAm (200 µmol)	$[Pd_2(\mathbf{L1})_4](NO_3)_4$ (2.50 µmol)	358.1 Pa	22

3 Chloride-triggered rearrangement of $[Pd_4(L1)_8]^{8+}$ into $[Pd_2(L1)_4Cl]^{3+}$

The chloride-triggered rearrangement of $[Pd_4(\mathbf{L1})_8](BF_4)_8$ was performed in an NMR tube and was tracked by ^{1}H NMR spectroscopy. Specifically, an NMR tube was filled with a solution of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$ in D_2O (500 µL, 2.5 mM), then 25 µL of a stock solution of NaCl (100 mM in D_2O, 2.0 eq.) was added and the mixture was equilibrated at RT for 30 min. ^{1}H NMR spectra were recorded before and after addition of NaCl.



Scheme S10. Chloride-induced rearrangement of $[Pd_4(\mathbf{L1})_8]^{8+}$ into $[Pd_2(\mathbf{L1})_4Cl]^{3+}$.

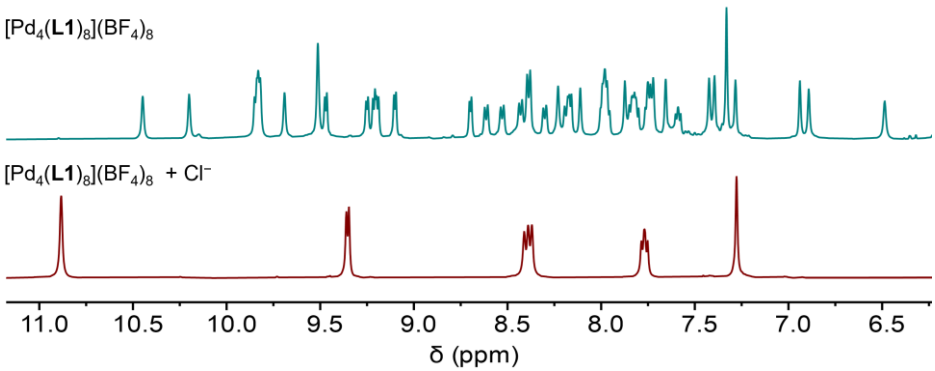
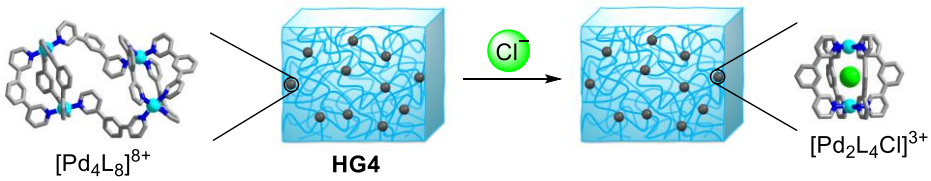


Figure S53. Aromatic region of the ^{1}H NMR spectrum (400 MHz, D_2O) of cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$ before (top) and after addition of chloride (bottom).

4 Chloride-triggered topology changes of HG4

An aliquot (12.5 µL) of a NaCl stock solution (100 mM in D_2O, 2.0 eq.) was added to an NMR tube containing half of the hydrogel **HG4** synthesized as described in Section 2.7 (theoretically a content of 0.625 µmol of $[Pd_4(\mathbf{L1})_8]$ $(BF_4)_8$). The mixture was incubated at room temperature for 2 d. Subsequently, a ^{1}H NMR spectrum of the hydrogel was recorded, and the mechanical properties of the hydrogel were examined by rheometry.



Scheme S11. Chloride-induced rearrangement of $[Pd_4(\mathbf{L1})_8]^{8+}$ into $[Pd_2(\mathbf{L1})_4Cl]^{3+}$in **HG4**.

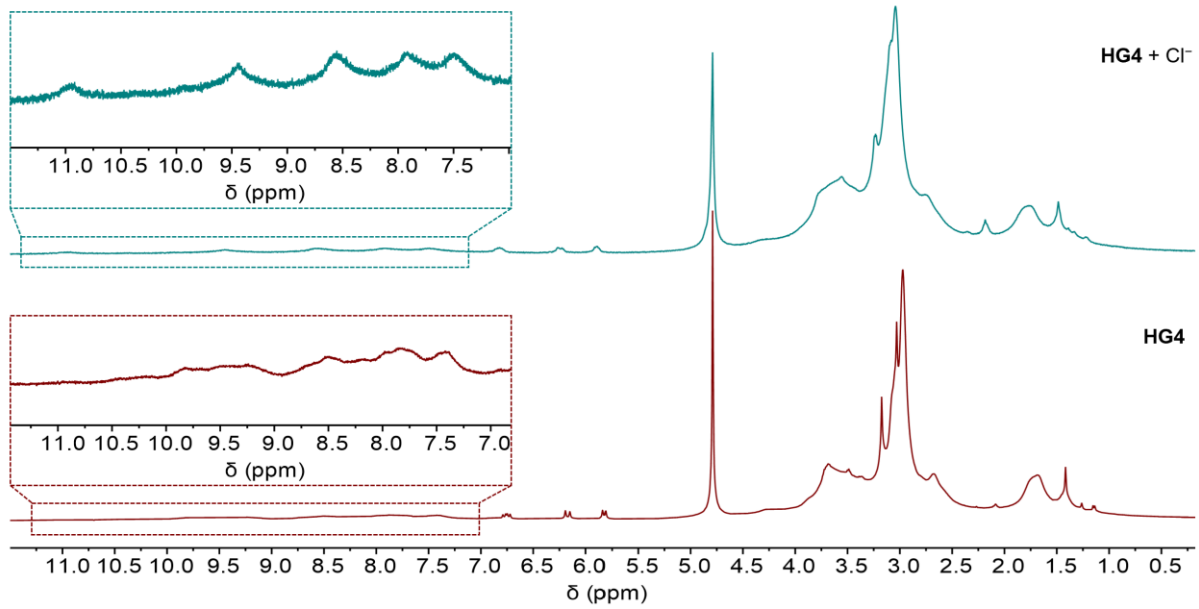


Figure S54. ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogels **HG4** before (bottom) and after addition of chloride (top).

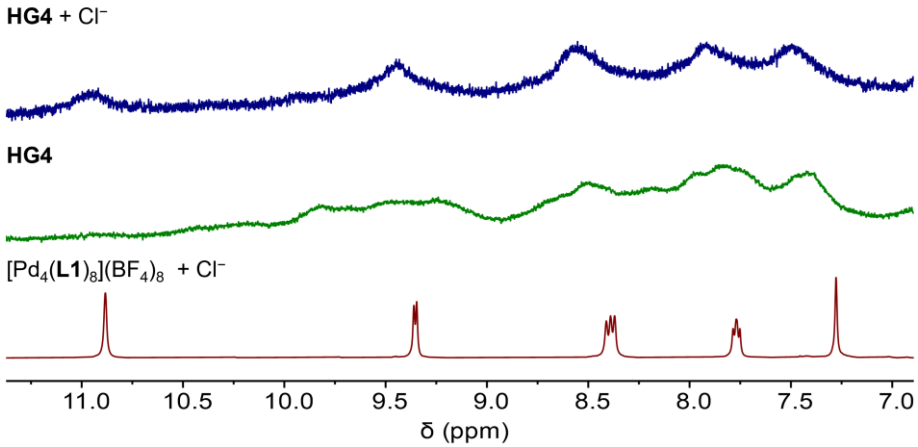


Figure S55. Aromatic region of the ^{1}H NMR spectrum (400 MHz, D_2O) of cage-crosslinked hydrogels **HG4** (middle), **HG4** after adding Cl^- (top), and cage $[Pd_4(\mathbf{L1})_8](BF_4)_8$ after adding Cl^- (bottom). The signal at ~ 11 ppm is indicative of the chloride-bound cage $[Pd_2(\mathbf{L1})_4Cl]^{3+}$.

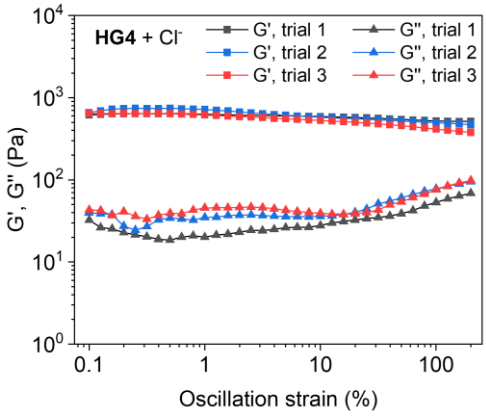


Figure S56. Amplitude sweeps in oscillatory rheology from 0.1% to 200% strain at frequency of 1 rad s^{-1} for **HG4** after treatment with chloride at 25 °C.

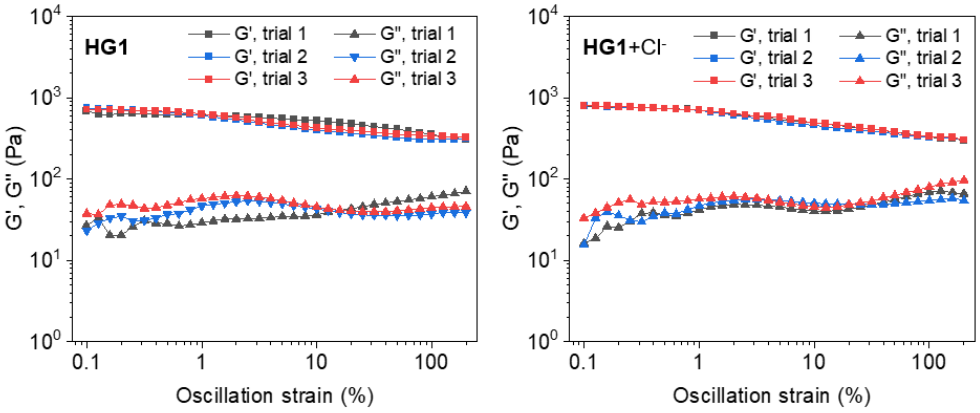


Figure S57. Amplitude sweeps in oscillatory rheology from 0.1% to 200% strain at frequency of 1 rad s^{-1} for **HG1** before and after incubation with NaCl (1 eq.) for 2 days at 25 °C.

5 Modeling detail

The starting geometry of $[Pd_4(\mathbf{L1^*})_8]^{8+}$ was constructed using software Avogadro 1.2.0,[3] with **L1*** being the non-pegylated analogue of ligand **L1**. The cage was then optimized at the GFN2-xTB[4] level using software xTB[4] in implicit acetonitrile treated with the analytical linearized Poisson-Boltzmann solvent model (ALPB).[5]

Table S4. Coordinates of the xTB-optimized structure of $[Pd_4(\mathbf{L1^*})_8]^{8+}$.

244
energy: -385.836591022043 gnorm: 0.000198069062 xtb: 6.6.1 (8d0f1dd)

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C	9.37342796046793	1.73536196827801	16.96039877119301
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C	8.68548483678100	-4.63617071719890	17.90103879832332
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C	3.72371351976820	-2.99411687761878	22.63219521331645
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H	7.42222636664036	1.76236749816953	20.46276158372289
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Pd	13.01738258503678	-3.77575842097331	29.04074797462599
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H	10.51338858196350	-4.28175875333482	30.33802834843213
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H	8.80796343095279	1.60584821882974	23.43972122471354

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